PRE-CONGRESS COURSE 6

On seeking and finding the evidence

Special Interest Groups Psychology and Counselling & Safety and Quality in ART
Munich - Germany, 29 June 2014

eshre
SCIENCE MOVING PEOPLE MOVING SCIENCE

On seeking and finding the evidence

Munich, Germany
29 June 2014

Organised by
The ESHRE Special Interest Groups Psychology and Counselling & Safety and Quality in ART

Contents

Course coordinators

Chris Verhaak (The Netherlands) and Petra de Sutter (Belgium) and Willianne Nelen (The Netherlands)

Course description

Finding evidence seems straightforward. Scientific guidelines are formulated, registers for RCTs are implemented. But what is the value of our evidence? How do patients perceive evidence? Why do they choose treatments without any evidence? What is the role of placebo? What is the role of communication in translating evidence to patient behaviour? These fundamental questions will be discussed from the perspective of patients, doctors, basic scientists, psychologists and yoga experts.

Target audience

Clinicians, counsellors, psychologists, paramedicals, basic researchers

Scientific programme

Chairmen: Uschi Van den Broeck – Belgium and Willianne Nelen - The Netherlands

09:00 - 09:30	Evidence: what does it mean? ***Cindy M. Farquhar - New Zealand***
09:30 - 10:00	The patient perspective ***Clare Lewis-Jones - United Kingdom***
10:00 - 10:30	When can we call an intervention established? ***Kelly Tilleman - Belgium***
10:30 - 11:00	Coffee break
11:00 - 11:30	Practitioners and guidelines: 10 tips for a happy marriage ***Willianne Nelen - The Netherlands***
11:30 - 11:45	Discussion
11:45 - 12:15	Decision making: how to balance evidence with patient preferences ***Jacqueline Pieters - The Netherlands***
12:15 - 12:30	Discussion
12:30 - 13:30	Lunch

Chairmen: Christianne Verhaak - The Netherlands and Petra De Sutter - Belgium

13:30 - 14:00	The Placebo effect: what is the role of suggestion in pain management ***Andrea Evers - The Netherlands***
14:00 - 14:15	Discussion
14:15 - 14:45	The art of medicine: communication or manipulation? ***Jan Kremer - The Netherlands***
14:45 - 15:00	Discussion
15:00 - 15:30	Coffee break
15:30 - 16:00	The Mindfulness Based Program for Infertility: evidence regarding its efficacy ***Ana Galhardo - Portugal***
16:30 - 17:00	Yoga: Its potential role in infertility management ***Rajvi Mehta - India***

ESHRE GUIDELINE:

// PSYCHOSOCIAL CARE IN INFERTILITY AND MEDICALLY ASSISTED REPRODUCTION

GET INFORMED

The draft of the guideline will be presented at the ESHRE Annual Meeting 2014 by Dr. Sofia Gameiro

Be there!
Monday 30 June
at 15:15, Room 5

GIVE YOUR OPNION!

The guideline will be open for external review after the annual meeting.

Take this opportunity to review the guideline and submit your comments!

For more information
check www.eshre.eu/guidelines
or email nathalie@eshre.eu

GUIDELINE GROUP

Sofia Gameiro (Chair), Jacky Boivin, Eline Dancet, Cora de Klerk, Marysa Emery, Clare Lewis-Jones, Petra Thorn, Uschi Van den Broeck, Christos Venetis, Chris Verhaak and Tewes Wischmann

Evidence – what does it mean?

Professor Cindy Farquhar
Fertility Plus
National Women's Health
University of Auckland
New Zealand

ESHRE Munich 2014

fertility PLUS

Statement of disclosure

- No commercial conflicts of interest for the past 10 years for the following
  - No travel grants from commercial groups
  - No consultancies from commercial groups
- Co-ordinating editor of the Cochrane Menstrual Disorders and Subfertility Group – funded by the NZ Ministry of Health

Outline

- A brief history of evidence in health care
- Heirachy of evidence
- GRADE
- Systematic reviews
- How we can use it everyday

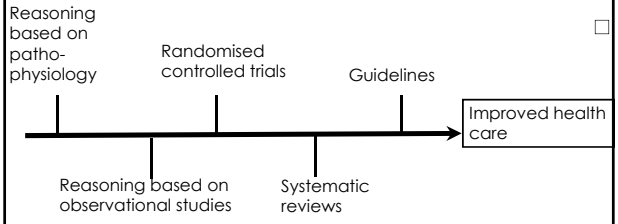
The delivery of health care is variable

- 30-40% patients do not get treatments of proven effectiveness
- 20-25% patients get care that is not needed or potentially harmful
  - Schuster et al 1998 Milbank Memorial Quarterly
  - R Grol 2001 Med Care
  - McGlyn et al 2003 NEJM
  - Sund et al JAMA
  - Grimshaw et al 2012 Implementation Science

Why do we need evidence for fertility treatments?

- Fertility treatments are costly and the stakes are high
- Are we offering our patients the most effective treatments?
- How do we know that we are not doing more harm than good?

There's been a culture change



A brief history of 'evidence' and health care

- Professor Gordon Guyatt
  - 1st used the term in an article in JAMA 1992
- In the preceding decade many others involved
  - Iain Chalmers, Kay Dickersin, Muir Gray, Brian Hayes, David Sackett, Drummond Rennie

Evidence based medicine

Evidence-based medicine is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients

Sackett et al BMJ 1996

Not just evidence…

Integrating individual clinical expertise

with

Best available clinical evidence from systematic research

Neither alone is sufficient

The Evidence Heirarchy

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GRADE Grading the evidence

- Grades quality of evidence

  AND

- Strength of recommendations

GRADE

Summary of GRADE approach to grading the quality of evidence

Table 2 A summary of the GRADE approach to grading the quality of evidence for each outcome

Source of body of evidence	Initial rating of quality	Factors that may decrease the quality	Factors that may increase the quality	Final quality of a body of evidence *
Randomised trials	High	1. Risk of bias 2. Inconsistency 3. Indirectness 4. Imprecision	1. Large effect 2. Dose–response 3. All plausible residual confounding would reduce the demonstrated effect or would suggest a spurious effect if no effect was observed	High (⊕⊕⊕⊕ or A) Moderate (⊕⊕⊕◯ or B)
Observational studies	Low	5. Publication bias		Low (⊕⊕◯◯ or C) Very low (⊕◯◯◯ or D)

*Quality of evidence definitions.
High: Further research is very unlikely to change confidence in the estimate of effect.
Moderate: Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low: Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very low: Any estimate of effect is very uncertain.

GRADING RECOMMENDATIONS

Table 3 Implications of the two grades of strength of recommendations in the GRADE approach

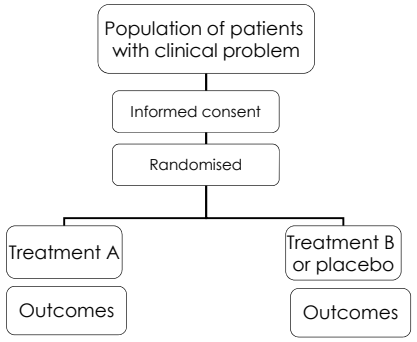
Target group	Strong recommendations*	Conditional (weak) recommendations
Patients	Most people in your situation would want the recommended course of action and only a small proportion would not	The majority of people in your situation would want the recommended course of action, but many would not
Clinicians	Most patients should receive the recommended course of action	Recognise that different choices will be appropriate for different patients and that you must make greater effort with helping each patient to arrive at a management decision consistent with his or her values and preferences Decision aids and shared decision making are particularly useful
Policy makers and developers of quality indicators	The recommendation can be adopted as a policy in most situations	Policy making will require substantial debate and involvement of many stakeholders

* Strong recommendations based on high quality evidence will apply to most patients for whom these recommendations are made, but they may not apply to all patients in all conditions; no recommendation can take into account all of the often-compelling unique features of individual patients and clinical circumstances.

Quality of evidence

- ✪✪✪✪ High
  - Further research is **unlikely to change** our confidence in the estimate of effect
- ✪✪✪ Moderate
  - Further research is **likely to have important impact** on confidence and **may** change estimate
- ✪✪ Low
  - Further research is **very likely** to have important impact and **is likely** to change estimate
- ✪ Very low
  - Any estimate of effect is **very uncertain**

The randomised controlled trial



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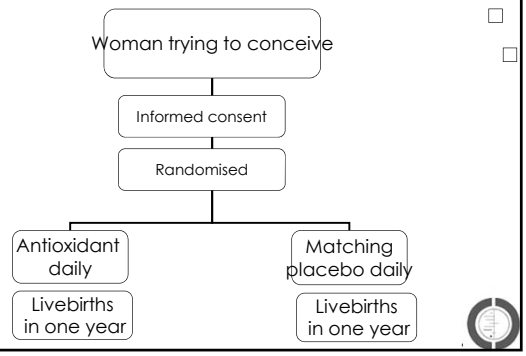
The randomised controlled trial



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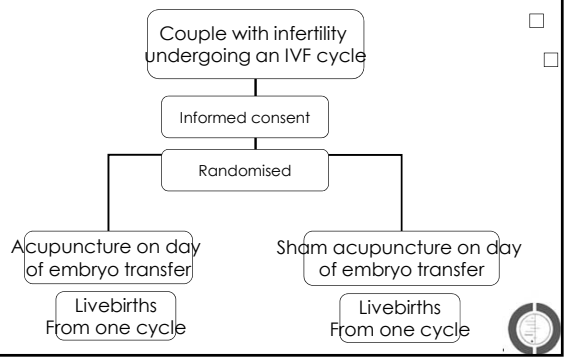
The randomised controlled trial



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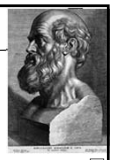
You don't need an RCT for everything…

- Insulin for ketoacidosis
- Penicillin for bronchopneumonia
- CPR for collapse
- IVF for tubal infertility
- Parachutes for jumping out of planes

Usually for areas where there is uncertainty or where the effects of health care are small…

First do no harm



"Because reviewers have not used scientific methods, advice on some life-saving therapies has been delayed for more than a decade, while other treatments have been recommended long after controlled research has shown them to be harmful".

***Antman** et al* 1992

It seemed like a good idea at the time….

- Blood letting
- Lobotomy
- Lying newborn infants prone
- Diethyl stilboestrol for recurrent miscarriage
- Thalidomide for nausea in early pregnancy

It seemed like a good idea…..

- ZIFT/GIFT
- Medical treatment for infertility and endometriosis
- Clomiphene citrate in unexplained infertility
- Follicular flushing during oocyte retrieval
- PGS for advanced maternal age in IVF cycles

PGS was the new breakthough for older women….

"this is going to make all the difference for older women…."

There was enthusiasm for PGS

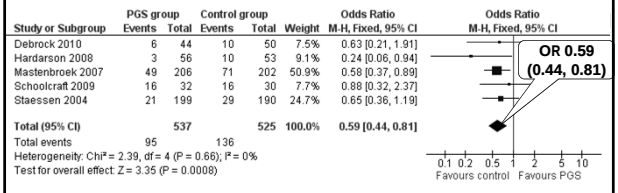
- Advanced maternal age
  - Gianaroli 1999, Munne 1999, Kahraman 2000, Obasaji 2001, Munne 2003; Montag 2004; Platteau 2005
- Repeated IVF failure
  - Gianaroli 1999, Kahraman 2000, Pehlivan 2003,Munne 2003, Wilding 2004
- Recurrent miscarriage
  - Pellicer 1999, Rubio 2003, Rubio 2005, Munne 2005
- Severe male factor
  - Silber 2003, Platteau 2004

Preimplantation genetic screening for abnormal number of chromosomes (aneuploidies) in in vitro fertilisation or intracytoplasmic sperm injection (Review)

Twisk M, Mastenbroek S, van Wely M, Heineman MJ, Van der Veen F, Repping S

- Cochrane review 1st published in 2005
  - Only one RCT
- Updated in 2010
  - 9 RCTs – 1589 women
  - All used FISH
  - 3 different populations

Preimplantation genetic screening for advanced maternal age – reduced live birth rates



Study or Subgroup	PGS group Events	Total	Control group Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Debrock 2010	6	44	10	50	7.5%	0.63 [0.21, 1.91]
Hardarson 2008	3	56	10	53	9.1%	0.24 [0.06, 0.94]
Mastenbroek 2007	49	206	71	202	50.9%	0.58 [0.37, 0.89]
Schoolcraft 2009	16	32	16	30	7.7%	0.88 [0.32, 2.37]
Staessen 2004	21	199	29	190	24.7%	0.65 [0.36, 1.19]
Total (95% CI)		**537**		**525**	**100.0%**	**0.59 [0.44, 0.81]**
Total events	95		136			

Heterogeneity: Chi² = 2.39, df = 4 (P = 0.66); I² = 0%
Test for overall effect: Z = 3.35 (P = 0.0008)

ESHRE PGS Consortium

- By 2008 over 16000 cycles of PGS were undertaken…
- Assuming a 20% live birth rate, it is estimated that between 640 to 1728 fewer babies born as a result

Advanced Access publication on February 2, 2010 doi:10.1093/humrep/dep476

human reproduction ESHRE PAGES

What next for preimplantation genetic screening (PGS)? A position statement from the ESHRE PGD Consortium steering committee†

Joyce Harper[1,12], Edith Coonen[2], Martine De Rycke[3], Francesco Fiorentino[4], Joep Geraedts[2], Veerle Goossens[5], Gary Harton[6], Celine Moutou[7], Tugce Pehlivan Budak[8], Pam Renwick[9], Sioban SenGupta[1], Joanne Traeger-Synodinos[10], and Katerina Vesela[11]

- The only effective way to resolve the debate is to perform more well-designed and well-executed clinical trials

ASRM Practice Committee 2008

- Available evidence does not support the use of PGS as currently performed to improve live-birth rates in patients with advanced maternal age or in patients with previous implantation failure.

Why observational studies are not good enough to guide practice?

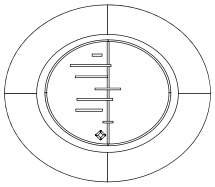
- Selection bias
  - Some reason patients are treated differently from each other
  - Leads to incorrect conclusions

Tools for evidence based medicine: systematic reviews ……

Key features of a systematic review?

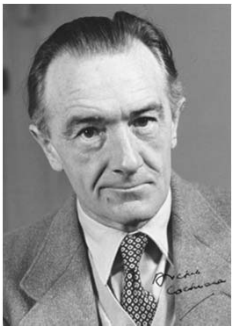
- clearly stated objectives
- pre-defined eligibility criteria
- explicit, reproducible methodology
- systematic search
- assessment of validity of included studies
- systematic synthesis and presentation of findings

The Cochrane Collaboration



Preparing, maintaining and disseminating systematic reviews of the effects of health care

Archie Cochrane's challenge



"It is surely a great criticism of our profession that we have not organised a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomised controlled trials."
Cochrane 1979

Photograph: Cardiff University Library, Cochrane Archive, University Hospital Llandough

Advantages of Cochrane reviews

- Updating of reviews regularly
- Methodologically robust
- Less likely to be biased

How do (Cochrane) systematic reviews reduce bias?

- Prestated methods published
- Limit publication bias
- Systematic methodology
- Limit commercial and industry sponsorship of reviews

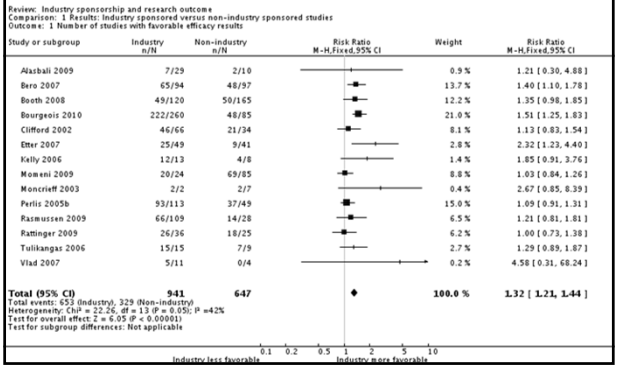
Better quality reviews

"..we observed far superior reporting standards of Cochrane reviews compared to non-Cochrane therapeutic ones."

"For therapeutic reviews, all the Cochrane ones reported assessing the quality of included studies whereas only half of the non-Cochrane did."

"The seven industry supported reviews that had conclusions recommended the experimental drug without reservations, compared with none of the Cochrane reviews, although the estimated treatment effect was similar on average

Studies with funding bias are more likely to have favourable results (Lundh et al 2012)



The Cochrane Menstrual Disorders and Subfertility Group

- 200+ systematic reviews on the Cochrane Library
- Editorial office at the University of Auckland
- Employ a Managing Editor and Trial Search Coordinator
- 26 editors – methodologists, statisticians, content experts
- Work with about 850+ authors

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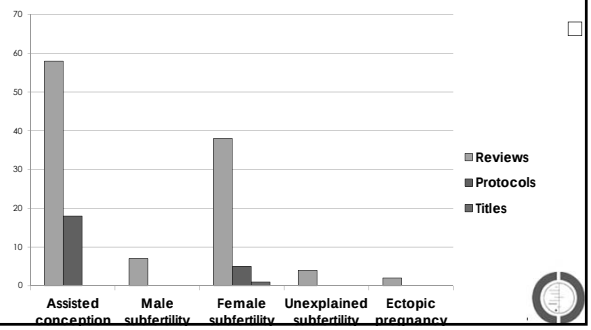
Subfertility Cochrane reviews by topic (August 2013) (n=110)



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The evidence challenge …

- Meeting our patients needs
  - Offering the best treatments
- Being up to date
  - Delays in dissemination
- Competing knowledge sources
  - Medical journals – single studies, reviews
  - Medical societies
  - Conferences
  - Industry information

By RYAN JASLOW / CBS NEWS / October 9, 2013, 4:15 PM

Endometrial scratching boosts IVF odds by 20 percent, says study

They found women who had the procedure had about a 49 percent rate of pregnancy, compared to 29 percent in the other group. Thirty-three of the procedures resulted in live births, Sky News reported.

The study has yet to be published, but the researchers hope to test more women until the study is released next year.

Should we offer endometrial injury before an IVF cycle?

- How many studies are there?
  - 5 randomised controlled trials
- Which study should I read?
  - The largest?
  - The most recent?
  - All of them….

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Or you could read a systematic review…

- Nastri *et al* Endometrial injury in women undergoing assisted reproductive techniques. Cochrane Library 2012

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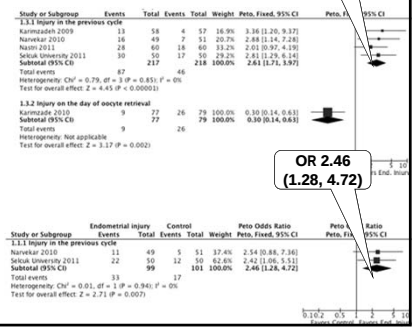
Endometrial injury

- Clinical pregnancy rate



- Live birth rate

But is there enough evidence….

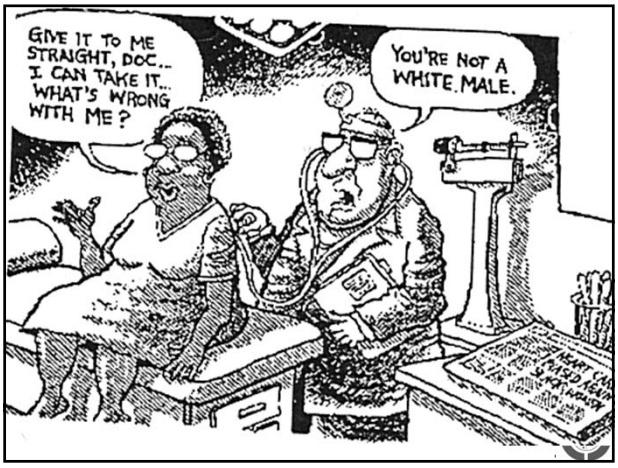
- 5 RCTs - 4 in preceding cycle and one on day of OPU
- All fresh transfers
- Only three report live birth
- All use multiple embryo transfer

Possible mechanisms for endometrial injury

- Inducing decidulisation? Barash 2003, Loeb L. 1907;18:563–5, Humphrey KW. 1969;22:689–99, Finn CA, Martin L. 1972;7:82–86.
- Inflammation? Injury causes a wound response with neutrophil activation that releases inflammatory mediators including cytokines, protease enzymes and growth factors etc. which may improve implantation
  - Gnainsky et al 2010
- Synchronisation? The wound response (from injury) may delay endometrial maturation, and improve synchrony (implications for frozen transfers)
  - Zhou et al, Li & Hao 2009

Applying this evidence to your patients/yourself?

- Which **p**atients?
  - Most of the women in the studies had recurrent implantation failure
- Which **i**ntervention?
  - Biopsy? Brush?
  - Timing? – preceding cycle? Cycle of pick up?
  - Number of embryos transferred
  - Fresh or frozen
- Which **o**utcome?
  - Live birth, clinical pregnancy, multiple pregnancy



Your patient

- 38 years old?
- One fresh transfer? After stimulated cycle with agonist down reg
- She has one frozen embryo to transfer

- In your clinic:
  - The chance of live birth after one frozen embryo is…….

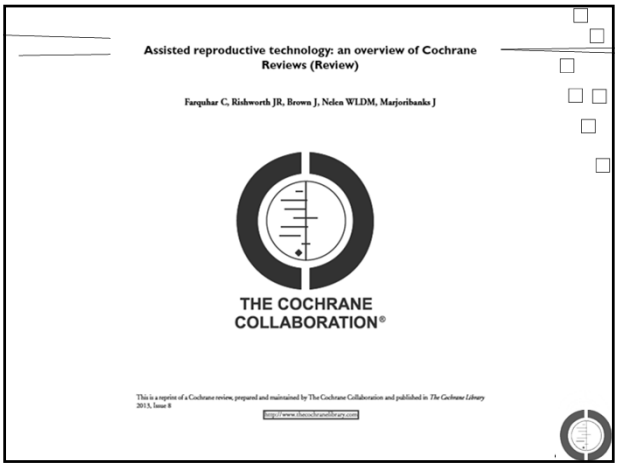
What is the harm?

- Perhaps the 'injury' is only effective in fresh transfers as that endometrium is different from non stimulated endometrium

Rationale for new RCT of biopsy and ART

Limitations of current evidence

- No frozen-thaw data → implications for mechanism
- Minimal single embryo transfer data
- Minimal live birth data
- Minimal data on non-recurrent implantation failure patients


Assisted reproductive technology: an overview of Cochrane Reviews (Review)

Farquhar C, Rishworth JR, Brown J, Nelen WLDM, Marjoribanks J

THE COCHRANE COLLABORATION®

This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2013, Issue 8

Cochrane ART overview – 2013

1. Indication for ART
2. Pre ART
3. Down regulation
4. Ovulation induction
5. Ovulation trigger
6. Oocyte retrieval
7. Sperm retrieval
8. Laboratory procedures
9. Embryo transfer
10. Luteal phase support
11. Preventing OHSS
12. Frozen embryo transfer

Description of included studies

- 54 Cochrane systematic reviews of subfertile couples undergoing ART.
- Overall review quality was high with 43/54 reviews meeting all AMSTAR criteria
- 32/54 reviews had conducted a search within the past 3 years

Outcomes reported in 54 reviews

Live birth rate	39 reviews
Clinical pregnancy rate	48 reviews
Ovarian hyperstimulation syndrome	21 reviews
Multiple pregnancy	24 reviews
Miscarriage	34 reviews

Farquhar C, Rishworth JR, Brown J, Nelen WLDM. Assisted reproductive technology: an overview of Cochrane Reviews [Protocol]. Cochrane Database of Systematic Reviews 2013, Issue [6].

Review findings

Effective interventions 17 reviews	Review found evidence of effectiveness or improved safety for an intervention
Promising interventions 13 reviews	Review found some evidence of effectiveness or improved safety for an intervention, but more evidence is needed
Ineffective interventions 3 reviews	Review found evidence of a lack of effectiveness or reduced safety for an intervention: 10 reviews
Possibly ineffective interventions 10 reviews	Review found evidence suggesting a lack of effectiveness of reduced safety for an intervention, but more evidence is needed: 3 reviews
No conclusions possible due to lack of evidence 11 reviews	Review found insufficient evidence to comment on the effectiveness or safety of an intervention.

www.cochranejournalclub.com

Examples of effective interventions

Endometrial injury performed in the month prior to ovulation induction for ART increases both the live birth rate and clinical pregnancy rate in women with recurrent implantation failure

Laparoscopic tubal occlusion is an alternative to laparoscopic salpingectomy in improving IVF pregnancy rates in women with hydrosalpinges

The administration of GnRHa for a period of 3-6 months prior to IVF or ICSI in women with endometriosis increased the odds of clinical pregnancy by fourfold

Increased live birth rate associated with embryo culture using low oxygen concentrations

Increase in clinical pregnancy rate using ultrasound guided embryo transfer compared with clinical touch

www.cochranejournalclub.com

Examples of ineffective interventions

Preimplantation genetic screening as currently performed significantly decreases live birth rates in women of advanced maternal age and those with repeated IVF failure. Trials in which PGS was offered to women with a good prognosis suggested similar outcomes

No evidence to suggest a benefit of using coasting to prevent OHSS compared with no coasting or other interventions

www.cochranejournalclub.com

Where are the research gaps ?

	Effective intervention	Promising interventions	Possibly ineffective	No conclusions possible
1. Indication for ART	0	1	0	2
2. Pre ART	4	2	3	2
3. Down regulation	3	0	1	0
4. Ovulation induction	2	5	1	1
5. Ovulation trigger	2	0	0	0
6. Oocyte retrieval	1	1	0	0
7. Sperm retrieval	0	0	0	1
8. Laboratory procedures	2	2	2	1
9. Embryo transfer	1	2	2	1
10. Luteal phase support	1	0	1	0
11. Preventing OHSS	2	0	1	0
12. Frozen embryo transfer	0	0	0	1

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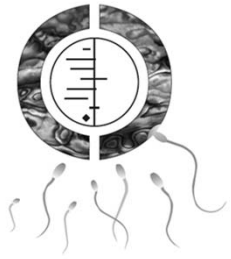
Systematic reviews in subfertility

- There are over 110 Cochrane reviews in subfertiilty and 54 are in an overview
- Useful for clinicians and patients seeking a summary of studies which have been graded
- Highlight gaps in research
- Working collaboratively with specialist groups to develop guidance for best practice

Evidence

- Needs careful appraisal by a group of experts and patients
- Should take the patients perspective
  - Live birth
  - Safety data
  - Satisfaction

Cochrane Menstrual Disorders and Subfertility Group



@CochraneMDSG www.cochrane.org

On seeking and finding evidence
The patient perspective

Clare Lewis-Jones MBE
Chair – Fertility Europe
and
Consultant to
Infertility Network UK

Commercial Relationships / Potential Conflict of Interest

- Infertility Network UK (I N UK) operate a corporate partnership scheme which offers different levels of partnership and allows companies to sponsor the charity's activities enabling the charity and corporate organisations to make an active and visible commitment to the development of high quality patient support and care. In the UK the Assn. of British Pharmaceutical Industries do not permit such companies to advertise their products to patients directly nor would I N UK agree to as we must remain independent.
- I N UK and our current corporate partners, Ferring Pharmaceuticals, Merck Serono, Auxogyn, Hologic, Gideon Richter, Casmed International and Access Fertility do not publicise their product to our members/beneficiaries

Learning Objectives

- Definition of Evidenced Based Medicine and the application of evidence
- Evidence of patient involvement in evidence based medicine
- Why should patients need evidence when presenting with possible fertility issues
- Patient centred care
- Why and when might patients need evidence when presenting with possible fertility issues
- Focus on single embryo transfer
- The role and importance of patient organizations' as a partner with clinics in improving the patient journey and experience
- The importance of emotional support and counselling for couples going through fertility treatment

Topics to be covered

- Definition of evidence based medicine
- Examples of patient involvement in evidence based medicine
- Why might patients need evidence when presenting with possible fertility issues?
- Patient centred care
- How patients source their own evidence and why
- The benefits of patients centred care
- Patient friendly care
- Why and when might patients need evidence when presenting with fertility issues
- Some feedback in relation to patient experiences at UK clinics
- Recommendations

Definition of Evidence Based Medicine

- **Evidence-based medicine** (**EBM**) is defined as "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.“
- This definition has since been adopted by major organizations, including the Cochrane Collaboration and the Centre for Evidence Based Medicine

Sackett DL et al 1996.

The application of evidence

- Dependent on the view of the clinician and the patients circumstances and preferences and is therefore subject to variation
- It remains subject to input from:
  - Personal
  - Political
  - Philosophical
  - Religious
  - Ethical
  - Economic
  - Aesthetic values.

Examples of patient involvement in evidence based medicine

Cochrane Consumer Network (CCNet)

- CCNet's primary role is to get healthcare consumers involved in the production of Cochrane Systematic Reviews.
- The most common role for consumers in the Collaboration is the Consumer Referee.

Consumer Referee

- The consumer referee improves the quality of Cochrane Reviews by:
- •Providing a consumer perspective by commenting on the "Plain Language Summary" of the review
- •Commenting on a Cochrane review of the best evidence on a healthcare intervention, prior to publication
- •Commenting on protocols to ensure that outcomes relevant to consumers are included
- •Preparing review summaries in plain language

National Institute for Health and Care Excellence (UK)

- The National Institute for Health & Care Excellence (NICE) have a "Patient and Public Involvement Policy
- Their approach is based on two key principles
  - That lay people and organisations representing their interests have opportunities to contribute to developing NICE Guidance, advice and quality standards and support their implementation, and
  - That because of this contribution, their guidance and other products have a greater focus and relevance for the people most directly affected by their recommendations

Background

- NICE guidance aims to improve quality by providing health and social care professionals, and patients and the public, with the information they need to make decisions about treatment and care
- All NICE recommendations are based on the best available evidence
- They consider the research on different types of treatment, interventions and care and how well they work and, in many cases, how much value they provide compared to their cost

Background - continued

- NICE Evidence Services is a service which enables people across the NHS and the wider public and social care sectors to access clinical and non-clinical evidence and information of the highest quality
- Patients, service users, carers and the public can be involved in producing and promoting their guidance, quality standards, as formal members of committees and working groups

NICE Clinical Guideline on Fertility treatment in the UK

- First guideline published February 2004
- Updated guideline published February 2013
- Based on both clinical effectiveness and cost effectiveness
- Lay version available online
- Patient representatives on both guidelines (including myself)
- Methodology: Literature search strategy
  - The aim of the literature review was to identify and synthesise relevant evidence within the published literature, in order to answer specific clinical questions.

http://guidance.nice.org.uk/CG156

Why should patients need evidence when presenting with possible fertility issues?

DXSummit.org Global Summit on Diagnostic Alternatives

- Article by Amy Price, research graduate student at Oxford University working on PLOT (Public-Led Online Trials) project
- "Open Data, Patient Perception and Experience With Evidence"

http://dxsummit.org/archives/1252

The Open Cure by Salvatore Laconesi

- Salvatore is an Italian tactical media artist diagnosed with brain cancer in September 2012

"The first thing you notice at the hospital is that they are not really talking to you. Medical language is difficult and complex, and they rarely take action to make things more understandable to you. … And in more than one way, it is an explicit evidence of the approach which medicine has towards patients: they cease to be "humans" and become sets of parameters on a medical record subject to certain protocols and standards"

Patrick Lichty. La Cura: An Open Source Cure

How do patients source evidence? And why?

- Those with fertility problems are often said to be the most informed group of patients
- Most are hungry for information and "look it up on the internet"
- Medical journals, text books, encyclopaedias, research papers and huge medical databases once available only to doctors are now just a mouse click away
- But some people still prefer to leave everything up to their doctor

Patient centred care

Definition of "Patient Centred Care"
The Institute of Medicine

"Care that is respectful of and responsive to individual patient preferences and needs and that is guided by patient values"

The King's Fund

"Patient centred care is multi-dimensional; it encompasses all aspects of how services are delivered to patients"

- Institute of Medicine offers this list:
  - Compassion, empathy and responsiveness to needs, values and expressed preferences
  - Co-ordination and integration
  - **Information**, communication and education
  - Physical comfort
  - Emotional support, relieving fear and anxiety
  - Involvement of family and friends

The patients' perspective on fertility care: a systematic review

E.A.F. Dancet et al 2010

- Results:
  - "Overall, fertility patients want to be treated like human beings with a need for: medical skills, respect, coordination, accessibility, information, comfort, support, partner involvement and a good attitude of and relationship with fertility clinic staff"

“Patient-friendly” procedures

- What does “patient-friendly” mean to patients?
  - Less drugs?
    - Natural or Mild IVF
  - Less painful procedures?
    - Injections
  - Fewer visits to the clinic?
    - “IVF in 2 weeks”

And/or?

- Clinic friendliness/understanding/time
- Safety versus success?
  - eSET
- Honest appraisal of a couples chance of success?
  - Based on evidence available from scientific studies
- Equity of access
- Cost of treatment?

Do different patients interpret patient “friendly” in different ways?

- Given the various hurdles patients encounter during a treatment cycle – some of which are more patient-friendly than others.
  - Some couples want to produce as many eggs as possible as they feel this gives them a better chance of success
  - Some women will perhaps feel that the egg collection was painful – some won’t
  - I would imagine most men would say surgical sperm retrieval is painful and not patient friendly! Whilst others would see it as just something they just have to get through.

Are patients really concerned about whether the treatment is “patient-friendly”?

- Or are they simply thankful that at least someone is willing to help them have a baby – no matter what that treatment entails in terms of safety/pain.
- Of course, this doesn’t mean to say that those providing the treatment – and patient organisations such as members of Fertility Europe - shouldn’t consider this aspect of fertility treatment

Safety and efficacy of treatment in relation to patient autonomy

- Health risks to patient and to potential child
- Willingness to take that risk if it has the remotest possibility of achieving their deep-rooted desire to have a child?
- Willingness to take further risks after failed treatment?

A patient’s response for feedback

“For me I never felt (not sure if I was a bit naïve) there were many risks to it, apart from the obvious one of how would we personally deal with the potential failure of a cycle, which was a huge one. I never felt at risk with the procedures or drugs as such. Although on my last go (3rd attempt) I was flagged up as at risk of OHSS which was worrying. I also had a couple of passing out episodes on this cycle at egg collection which was quite daunting. I never really thought too much about the risks of multiple births either. To be honest I think the subject was skimmed upon at the clinic, but to be fair I could have asked for more info too!”

Why and When might patients need evidence when presenting with possible fertility issues?

Has the patient been fully investigated?

- Patients should be informed what investigations are needed and why
- Backed up by evidence/information
- Patients need a care programme so that they know what is going to happen, when and why (evidence)
- Cost implications if applicable

Patients need to know what treatment options are available and recommended

- Male Factor infertility
  - If ICSI is not being recommended
    - Explanation as to why backed up by evidence
  - If ICSI is recommended
    - Explanation of diagnosis and recommendation of ICSI backed up by evidence of why ICSI is being recommended
    - Information on the success rates at clinic and information given on where to find this information for other clinics
  - Cost implications if applicable

Patients need to know what treatment options are available and recommended

- If DI is recommended
  - Explanation of diagnosis and recommendation of DI backed up by evidence of why DI is being recommended
  - Information on the success rates at clinic and information given on where to find this information for other clinics
  - Information on donors
  - Cost implications if necessary

Patients need to know what treatment options are available and recommended

- Female factor infertility
- If IVF/IUI/Egg Donation is recommended
  - Explanation of diagnosis and recommendation of IVF backed up by evidence of why the treatment is being recommended
  - Information on the success rates at clinic and information given on where to find this information for other clinics
  - Information on egg donors if applicable
  - Cost implications if necessary

Single Embryo Transfer

- eSET
  - Reducing risk of conceiving a multiple pregnancy thus more “patient-friendly” in terms of safety
  - Reducing chances of conceiving – even slightly – is not considered “patient-friendly” by many patients – certainly in the UK.
  - Has caused enormous anger amongst many patients in the UK

Evidence for patients on the use of Single Embryo Transfer

- The Human Fertilisation & Embryology Authority (HFEA) in the UK introduced a policy on single embryo transfer in 2010
- Funded by the Department of Health, Infertility Network UK produced 2 factsheets on Single Embryo Transfer
  - One for patients: http://www.infertilitynetworkuk.com/uploaded/Fact%20Sheets/I%20N%20UK%20SET%20Patient%20Factsheet%20July%202013.pdf
  - One for health professionals http://www.infertilitynetworkuk.com/uploaded/Fact%20Sheets/I%20N%20UK%20SET%20HP%20Factsheet%20July%202013.pdf

One at a Time website – providing evidence

The funding of fertility treatment affects patients views/decision making

- In the UK it is estimated that approx. 70-80% of IVF takes place in the private sector
- Poor NHS funding leading to “Treatment by Postcode” or “Treatment by bank balance”
- Feel they need to take these risks – particularly if they can only afford to pay for one cycle of treatment
- If a patient is paying for their treatment should they have more say in that treatment?

Loss of patient autonomy

"I am one of the vast, vast majority who has paid for my own treatment (it's cost me about £25k to get this far) and I resent a government (who have taken money for each of these cycles in the form of the HFEA fee) decreasing my chances of success in this way.
By all means publicise the risks more (like the warnings on cigarette packages) but do not take away the right to choose"

Patient-centred infertility care: a qualitative study to listen to the patient's voice

Dancet, E A F et al 2011

- Method: 14 focus group discussions were organised with patients (*n* = 103) from 2 European countries to find out about patients' positive and negative experiences with infertility care
- Results: The patient-centredness of infertility care depends on 10 detailed dimensions, which can be divided into system and human factors, and there is two-way interaction between both kinds of factors

System factors

(In order of patients priority)

1. Provision of information
2. Competence of clinic and staff
3. Coordination & integration
4. Accessibility
5. Continuity and transition and physical comfort

Dancet, E A F et al 2011

Human factors

(In order of patients priority)

1. Attitude of and relationship with staff
2. Communication
3. Patient involvement and Privacy
4. Emotional support

Dancet, E A F et al 2011

Conclusions

- "This study provides a details patient's perspective of the concept "patient-centred infertility care" and an interaction model that aids understanding of the concept."
- "Fertility clinics are encouraged to improve the patient-centredness of their care by taking in to account the detailed description of the dimensions of patient-centred infertility care, and by paying attention to both system and human factors and their interaction when setting up "patient-centred improvement projects."

Dancet, E A F et al 2011

"Patients' attitudes to medical and psychosocial aspects of care in fertility clinics: findings from the Copenhagen Multi-centre Psychosocial Infertility (COMPI) Research Programme"

L. Schmidt et al 2003

- 2250 patients responded – 80% response rate
  - Vast majority considered a high level of medical information and patient-centred care as important
  - Fewer felt that professional psychosocial services were important and/or had the intention to use these services

Conclusions

- A supportive attitude from medical staff and the provision of both medical and psychosocial information and support should be integral aspects of medical care in fertility clinics.
- Although only a minority of the participants perceived professional psychosocial services as important, they should be available for patients whose infertility causes them much strain, especially for patients whose marital relationship suffered much because of infertility

L. Schmidt et al 2003

With apologies to UK clinics…

- Results of complaints received by the Human Fertilisation & Embryology Authority 2007/08
  - Attitude (Human factor – Priority 1) 1
  - Response (Human factor – Priority 1) 1
  - Incident (System factor – Priority 2) 2
  - Consent (Human factor – Priority 2) 3
  - Finance & Administration (System factor – Priority 1) 7
  - **Information (System factor – Priority 1) 8**
  - Other 8
  - Consultation Inc. clinical treatment (Human factor – Priorities 1 & 2; System factor – Priority 2) 30

Information

- Conflicting information regarding sperm donation
- Overwhelming quantity of information
- Insufficient information regarding failed/abandoned cycles
- Lack of information and lack of staff concern
- Incorrect and lack of information

Consultation and Clinical treatment

- Concern about type of treatment offered
- Insufficient information regarding donor anonymity
- Donor details requested 5 months late
- Poor treatment
- Centre did not act in best interests of patients
- After care following treatment
- Doctor didn't know patient and provided incorrect information

Recurrent theme

- Matches closely the issues raised by patients in general feedback to the HFEA
- In particular the quality and timeliness of information and emotional support received

Discussion

- Complaints remain low in relation to number of treatments per year – are patients nervous of complaining?
- Rushed consultation and a lack of understanding or empathy and failing to listen to patients is a common complaint about consultation with clinicians
- Complaints also arise because of differences in diagnosis when patients change to another clinic
- Lack of clarity and information for patients about costs – hidden extras e.g. scans/blood tests

Patient Organisation websites

- Full of information
- Relevant to their country
- Chat rooms
- Forums
- Need to be carefully managed/transparent/impartial
- Fertility Europe website www.fertilityeurope.eu

Some ideas

How should patients perceive evidence?

- Research is needed on how patients perceive evidence!
- Patients should not accept something they read/see as definitive
- Their clinician should help to make sense of the information they have sourced
- Need to form a partnership between the patient and the clinician
- But it should be a partnership of well informed equals
- The information should help to improve communications between patient and clinician – not replace it!

How Can Clinics Help "Get It Right" for the Patients?

- Information

•Give patients written information on all aspects of their investigations/treatment including the evidence right the way through their time at the clinic in a range of languages/formats
•Responsible use of the Internet
- Costed treatment plans
- Information evenings

How Can Clinics Help "Get It Right" for the Patients?

- Communication

- Ensure patients know who to contact if they have questions/concerns
- Responsible use of the internet
- Access to a counsellor - within the clinic and externally

Counselling

- Should be available at ALL clinics
- Should be available at all stages of treatment - i.E. Before, during and after
- Basic training in counselling for ALL clinic staff
- Leaflet explaining benefits of counselling and how to access it given to all patients

Time

- The most expensive thing of all, but almost the most important

How Can Patient Organisations Help?

- ☎Access to personal experiences
- ☎Access to good and impartial information
- ☎Websites with interactive chat rooms and forums – must be managed efficiently
- ☎Self-help
- ☎Mutual help
- ☎Removes the feelings of isolation

What information do patients need?

- Clinics must remember that their patients are people – and not numbers
- Clinics to be consistent
- Clinics to have standardised information based on evidence including how to source that evidence

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Thank you

When can we call an intervention established?

Kelly Tilleman, PhD

ESHRE Munich 2014

Based on the position paper from the SIGs Ethics and Law & Quality & Safety [1]

Veerle Provoost, PhD

When can we call an intervention established?

Conflicts of interest:

None

When can we call an intervention established?

Learning objectives:

1) Experimental ⟷ Established
2) The special case of oocyte vitrification
3) Problematic dichotomy
4) Alternative frame work as a solution: presentation of the tool
5) An experiment to see if this innovative tool is already established

1) Experimental ⟷ Established

American Society of Reproductive Medicine (ASRM):

> *A procedure for the treatment of infertility is considered experimental until there is adequate scientific evidence of safety and efficacy from appropriately designed, peer-reviewed, published studies by different investigator groups (ASRM, 2008)* [2].

> 'Adequate scientific evidence': *sufficient published medical evidence regarding the risks, benefits, overall safety and efficacy of the procedure in order to regard a procedure as established medical practice* (ASRM, 2009; ASRM, 2013) [3,4].

2) The special case of oocyte vitrification

J Assist Reprod Genet (2010) 27:69–74
DOI 10.1007/s10815-009-9382-y

FERTILITY PRESERVATION

Oocyte cryopreservation: is it time to remove its *experimental* label?

Nicole Noyes · Jeffrey Boldt · Zsolt Peter Nagy [5]

© http://www.ivfpodcasts.com/IVF_Podcasts/Podcasts.php?Oocyte-Vitrification-15

2) The special case of oocyte vitrification

data is reported, the technology's *experimental* label and the need for it to be performed under the auspices of an IRB should be reconsidered. We argue that OC could potentially now be deemed a standard ART procedure offered to appropriate patients after comprehensive informed consent once individual IVF clinics have established their own efficacy in the procedure.

Oocyte cryopreservation is not *experimental*

In a recent ASRM publication (June 2008), the Society defined an "experimental" procedure, indicating that one should be designated as such until "there is adequate scientific evidence of safety and efficacy from appropriately designed peer-reviewed published studies by different investigator groups". Three comparative studies regarding the efficacy of OC have now been published and several more are ongoing or in submission.

2) The special case of oocyte vitrification

Fertil Steril. 2011 Aug;96(2):277-85. doi: 10.1016/j.fertnstert.2011.06.030. Epub 2011 Jun 30.

Clinical application of oocyte vitrification: a systematic review and meta-analysis of randomized controlled trials.

Cobo A[1], Diaz C. [6]

CONCLUSION(S): Vitrification is an efficient method to preserve oocytes, although more large controlled clinical trials are needed to strengthen this conclusion.

ASRM Removes "Experimental" Label from Oocyte Cryopreservation

October 22, 2012

The Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology have released new practice guidelines that remove the "experimental" label from oocyte cryopreservation. "Although data are limited, no increase in chromosomal abnormalities, birth defects, and developmental deficits has been reported in the offspring born from cryopreserved oocytes when compared to pregnancies from conventional IVF/ICSI and the general population. Evidence indicates that oocyte vitrification and warming should no longer be considered experimental."

2) The special case of oocyte vitrification

American Society of Reproductive Medicine (ASRM):

> *A procedure for the treatment of infertility is considered experimental until there is adequate scientific evidence of safety and efficacy from appropriately designed, peer-reviewed, published studies by different investigator groups (ASRM, 2008)* [2].

'Adequate scientific evidence': *sufficient published medical evidence regarding the risks, benefits, overall safety and efficacy of the procedure in order to regard a procedure as established medical practice* (ASRM, 2009; ASRM, 2013) [3,4].

3) Problematic dichotomy

Dichotomy between

experimental and established treatment

3) Problematic dichotomy

Ann Oncol. 2014 Apr;25(4):896-901. doi: 10.1093/annonc/mdu027. Epub 2014 Mar 10.[7]

How can communication by oncologists enhance patients' trust? An experimental study.

Hillen MA[1], de Haes HC, Stalpers LJ, Klinkenbijl JH, Eddes EH, Butow PN, van der Vloodt J, van Laarhoven HW, Smets EM.

CONCLUSION(S): As hypothesized, oncologists can influence their patients' trust by enhanced conveyance of their level of competence, honesty, and caring. Caring behavior has the strongest impact on trust. These findings can be translated directly into daily clinical practice as well as in communication skills training.

Established?

3) Problematic dichotomy

- Problems with the dichotomy
  - No adequate account of the reality in the clinic
  - Several negative effects for the patient
  - Centers offering newly established treatments may do this without critically examining the effects

4) Alternative frame work as a solution

Experimental treatment → **Innovative treatment** → **Established treatment**

4) Alternative frame work as a tool

From experimental to established:

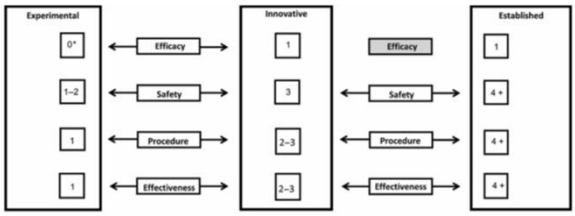
- A continuum of progression of a new procedure from the start as experimental treatment
- Innovative treatment as an intermediate category:

  A phase between experimental and established treatment

- Four criteria, each with their own threshold:
  - Efficacy
  - Safety
  - Procedure
  - Efficiency

4) Alternative frame work as a tool

A sequential four-criterion tool to assess new treatments or technologies:



4) Alternative frame work as a tool

Criterion	Definition	Scoring
Efficacy	Proof of principle	0. no proof of principle has been demonstrated 1. proof of principle has been demonstrated
Safety	The safety of the procedure, referring to the patient as well as the future children (not limited to data at birth).	1. considered safe in animals 2. reassuring preclinical data 3. reassuring short term data in human (up to at least three months post-delivery) in peer reviewed journals 4. reassuring mid-term data in human (up to at least five years post-delivery and including data on psychological development) in peer reviewed journals 5. reassuring long-term data in human (up to at least 25 years post-delivery, including data on psychological development and preferably on fertility) in peer reviewed journals
Procedure	The criteria in 'procedure' take into account the similarity or variability of the procedure in different laboratories.	1. no procedure has been described yet, or the procedure varies enormously between laboratories 2. technical performance of the procedure is highly variable between laboratories 3. technical performance of the procedure is relatively comparable between laboratories 4. technical performance of the procedure is highly comparable between laboratories 5. the procedure is considered a routine technique throughout different centers with common technical performance
Effectiveness	The likelihood of producing the desired outcome compared to outcome of conventional, established ART techniques	1. completely unknown, doubtful, or extremely low 2. low 3. reasonable 4. accepted but not as high as established ART treatment 5. as high or higher than established ART techniques

4) Alternative frame work as a tool

Experimental treatment

Conditions:

- At least clinical embryology data that indicate normal cleavage, embryo morphology and blastocyst formation
- Preferably shown safe in animals
- Always embedded in a research setting
- Offered to a selected and limited patient cohort
- Approved by a local ethics committee
- Informed consent of the patient: clear and neutral information.

4) Alternative frame work as a tool

Innovative treatment

- Only to be offered when data from experimental treatment have shown:
  - Proof of principle (efficacy)
  - Reassuring in terms of safety and efficacy
  - Based on a procedure specified in sufficient detail and with limited technical variability
- These data must have been obtained in studies with sound methodologies and published in peer reviewed journals
- Patients to whom innovative treatment is offered, should be offered clear information

4) Alternative frame work as a tool

Providing innovative treatment means commitment to systematically and uniformly collect data on procedures and outcomes

- Specific approval of a local ethics committee is advisable (in a general form) but not needed
- Data gathered should be made available to the scientific community regardless of the success of the treatment.

4) Alternative frame work as a tool

Established treatment

- When multi-centered data is published in peer-reviewed journals, on the basis of which it is regarded as a safe and efficient therapy. Ideally, based on prospective randomized trials.
- When procedures are performed according to a standard protocol

Follow-up is still required in order to monitor long-term (ideally transgenerational) health effects, including fertility and mental health.

Always be prepared to invalidate treatment when proven problematic

4) Alternative frame work as a tool

Procedures moving from experimental to established treatment over time.

Innovative treatments would be preceded by at least a limited experimental phase.

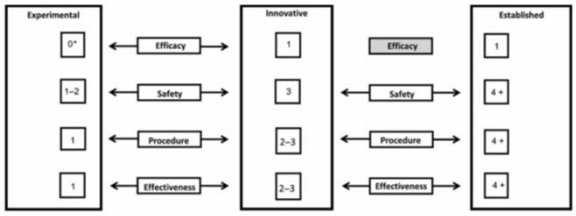
The more a procedure moves on the continuum, the higher the increase will be in what is known about its safety and efficiency while the procedural variability would decrease.

4) Alternative framework as a tool

A tool to facilitate the discussion

- To be used in a flexible way
- Experts may vary in their evaluation of specific techniques

5) Do the experiment!



man, vrouw en kind
Universitair Ziekenhuis Gent

Thank you!

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Practitioners and guidelines

10 tips for a happy marriage

Willianne Nelen, MD PhD

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- No conflict of interest

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Learning objectives

- Clinical Guidelines
- Clinical Guideline Development
- 10 tips
  - Barriers and facilitators
  - Role of evidence
  - Patient participation
  - Implementation

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Clinical Guidelines

- **Systematically developed** statements to assist **care providers** and **patient** in making decisions about appropriate health care for **specific clinical circumstances**

Field & Lohr1992

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Clinical Guidelines

- Can bridge the gap between evidence and clinical practice

- Decrease variation in care
- Increase efficiency of care
- Convince policy makers

↓

- Improvement quality of care

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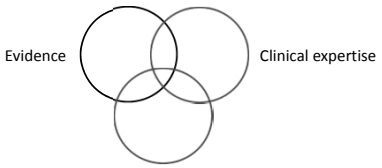
Clinical Guidelines

- No 'cook book'



Haynes, et al. 1996

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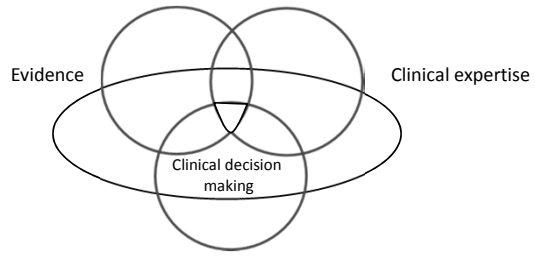
Clinical Guidelines



Haynes, et al. 1996

Evidence-based Clinical Guidelines

- Scientific evidence available: priority
- Preferably integration
  clinical expertise, patients' preferences
- Low level or no evidence available: more weight to clinical expertise and patients' preferences
- Evidence based vs. consensus based recommendations visible
  NICE
  ESHRE

Evidence-based Clinical Guidelines

Guidelines should be of high quality:

- valid
- reliable
- applicable
- clear
- timely revised
- …….

AGREE

- framework for appraising and guideline development

www.agreetrust.org

Evidence-based Clinical Guidelines

AGREE II:
6 domains – 23 items

- Scope and Purpose
- Stakeholder involvement
- Rigour development
- Clarity & Presentation
- Applicability
- Editorial independence

New version 2013

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Barriers Clinical Guidelines

- Clinical guidelines
  Applicability recommendations, availability of evidence, ambiguous recommendations
- Professionals
  Awareness, attitude, self-efficacy, routines, outcome expectancy, agreement recommendations
- Patients
  Patient characteristics, preferences, comorbidities
- Context
  Resources, time, reimbursement

Cabana et al. 1999
Lugtenberg et al. 2009

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Barriers Clinical Guidelines

Variation between guidelines

- Clinical guidelines
- Professionals 30-40%
  Education, uncertainty outcome, disagreement recommendation
- Patients 40-45%
  Characteristics, preferences
- Context 50-75%
  Financial issues, absence local protocol, lack of leadership

Haagen et al. 2005
Van Peperstraten et al. 2008
Van den Boogaard et al. 2011

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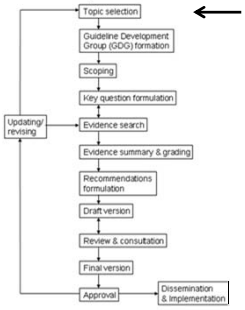
Guideline development



Topic selection

- Clinical problem (not a treatment/technique)
- Relevant clinical problem
  High volume, high costs, high patient impact,
- Benefits guideline
  Reduction practice variation, efficiency of care, patient-centred care
- Existing guidelines
- Existing evidence
  A lot of evidence vs. no evidence

ESHRE manual guideline development 2013

Topic selection

- Clinical problem (not a treatment/technique)
- Relevant clinical problem
  High volume, high costs, high patient impact,
- Benefits guideline
  Reduction practice variation, efficiency of care, patient-centred care
- Existing guidelines
- Existing evidence
  A lot of evidence vs. no evidence

ESHRE manual guideline development 2013

Guideline development group

- Participation representatives of all key disciplines
  - Content expert(s)
  - Methodological expert(s)
  - Non-expert clinician(s)
  - Allied health care provider(s)
  - Patient involvement
- Mandated by their group e.g. SIG, national society
- Disclosure conflicts of interest
- No industry representatives

ESHRE manual guideline development 2013
Standards Institute of Medicine 2011

eshre Radboudumc

Guideline development group

- Chairperson
  - Respected content expert
  - Good team-working skills
  - Aware of the group's skill mix

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Patient participation

- 'Effective participation of patient representatives should be adopted by guideline development groups'

Standards Institute of Medicine 2011

ESHRE
- Patient involvement important to ensure reflection of their needs, concerns and preferences
- Member guideline development group
- Consultancy patients' associations in different phases
  Scoping – review – implementation

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Patient participation

- Successful participatory tool for patient participation

- Wiki
- In collaboration Freya
- 298 unique visitors
- 289 recommendations
- Prioritized top 5
- Integration in a national guideline
- Visible as level P

Den Breejen et al. 2012

Scoping

Defining
- Overall objectives e.g. Cost effective care

- P Target patient population e.g. age, primary infertility
- I Interventions of interest e.g. IVF, PGD
- C Comparison e.g. no treatment
- O Outcomes e.g. ongoing pregnancy and complication rates

- Target users e.g. embryologists, gynaecologists, nurses
- Healthcare setting e.g. legislation, secondary or tertiary care
- Issues for patients' preferences e.g. mild ovarian stimulation or twin pregnancies

- Result: key questions

Evidence search

- 'literature searching is the key step in developing valid guidelines'
- incomplete or biased literature evaluation leads to inappropriate recommendations

- Systematic process to minimize bias and to be reproducible

- Can be outsourced by a methodological expert
  - Input from content experts
  - Definitive sifting by content experts
  - Completeness checked by content experts

ESHRE manual guideline development 2013
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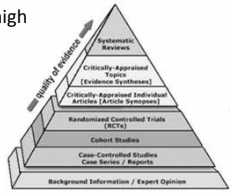
Evidence grading

Each recommendation is linked to:
- Summary of relevant evidence
  - Content
  - Quality
  - Completeness
  - Consistency

Guyatt et al. 2011
ESHRE manual guideline development 2013
Standards Institute of Medicine 2011

Evidence grading

- Rating level of evidence (GRADE)
- Level I – A - high



- Level IV - D - very low

Balshem et al. 2011
ESHRE manual guideline development 2013
Standards Institute of Medicine 2011

Evidence grading

- Rating strength recommendation (GRADE): strong / weak
  - Quality of evidence,
  - Balance benefits versus harms
  - Patient values
  - Acceptability stakeholders
  - Resource use
- Framework DECIDE/GRADE working group
- High level of evidence – weak recommendation is possible

Treweek et al. 2013
Andrews et al. 2013
ESHRE manual guideline development 2013
Standards Institute of Medicine 2011

Consensus recommendations

- Support different stakeholders
  - Guideline development group
  - External review
    - All relevant stakeholders
    - General public included
    - Consider all comments (written record)
  - Executive Committee

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Standards Institute of Medicine 2011

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Consensus recommendations

- Recommendations stand alone statements (complete sentences)
- Standardized format
  five 'W' rule: who does what for whom, when and in which way.
- Understandable (unambiguous) and answering the key questions
- Easy to translate into clinical practice
- Standardized phrasing

ESHRE manual guideline development 2013
Standards Institute of Medicine 2011

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Consensus recommendations

Standardizes phrasing
- Strong recommendation
  Clinicians should (not)
  It is (not) recommended
  It is (not) indicated
- Weak recommendation
  Clinicians might/may/could consider
  It is probably/conditionally recommended
  It is suggested

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Dissemination and Implementation

Dissemination
- Awareness - Announcements
  - Focus on Reproduction
  - ESHRE newsletter
  - annual meeting
  - National Societies and additional are separately informed

- Accessibility – Publications

Website

Hum Reprod

Clearinghouse/GIN library

Dissemination and Implementation

Implementation
- Guidelines are not self-implementing!

- Local ownership crucial e.g. translation into local protocol

  'Globalize the evidence, localize the decision'

Eisenberg et al. 2002

Dissemination and Implementation

Implementation
- Options tailored interventions

- No general strategy
  - Each implementation strategy is effective under certain circumstances
  - Multifaceted approach seems to be more successful
  - Implementation of individual recommendations more feasible

Grimshaw et al. 2004

Dissemination and Implementation

- Endometriosis app
- Patient version

Update

- 'Literature should be monitored regularly following publication'

ESHRE
- Every two year search for new evidence
- Original search strategies

- Update if new evidence suggests modification recommendation(s)

- Modules

Shekelle et al. 2001
ESHRE manual guideline development 2013
Standards Institute of Medicine 2011

Medico-legal implications

- Ongoing concern
- Clinical guidelines aid to clinical judgement no replacement

Moses et al. 2008

Happy marriage?

Practitioners – clinical guidelines
- Up to you!

Helpful
- make appropriate health care decisions
- bridge the gap evidence - clinical practice
- convince policy makers

Requirements
- Rigour development
  - AGREE instrument
  - Overcoming barriers
  - Evidence - Patients' preferences – Clinical expertise
- Dissemination and implementation

Thank you for your attention

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ESHRE Munich 29-06-2014

Decision making: how to balance *evidence* with patient *preferences*

Parents' perspective of unexpected fetal diagnosis after routine prenatal testing

Jacqueline Pieters, MD PhD
gynaecologist

MEDISCH CENTRUM KINDERWENS

The Netherlands

Disclosure

I have no commercial relationships or other activities that might be percieved as a potential conflict of interest related to this presentation

Learning objectives

- unexpected findings in prenatal tests: what are the incidences?
- new techniques are able to avoid unexpected findings, is that advisable?
- prenatal finding of a sex chromosomal aneuploidy: what is the prognosis for the child?
- pre- and post-test counseling: what is the role for the professional?
- parental decision-making, what are there emotions, how do they decide?

Evidence vs patient preference

Evidence:
prenatal diagnostic tests:

Trisomy 21/13/18/ 45,X/ 47,XXY/ 47,XXX
→ 80% of chromosomal anomalies

➢ Parents want to exclude Down syndrome (47,XX+21)

Sex chromosomal aneuploidy is the most common chromosome-abnormality at birth

1. Overall incidence: 1/400
2. Incidence in amniocentesis in >35 years: 1/250
3. 25% of chromosome abnormalities in amniocentesis= sex chromosome abnormality

➢ Sex chromosome abnormalities are often not discussed in pre-test counseling

Patient preference:
decision-making on Down syndrome

Linden et al, 1996; van Zwieten et al, 2004; Leung et al, 2008

On seeking and finding the evidence…

- How do patients perceive evidence in prenatal testing?
- What is the role of communication in translating the prenatal diagnosis to parents?
- How do they seek more evidence?
- How do they value professional advice?
- What is important in their decision-making?

"Unexpected findings" in prenatal testing

What are unexpected findings?

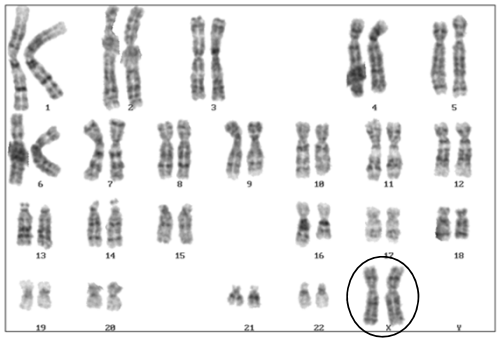
• *Unexpected* *for the professional* / *for the patient*

"unexpected findings are unwanted and unaimed for, as such they differ from standard test results"

Why are they interesting?

with new techniques, we can avoid them,
but is that a wise thing to do?

Full karyotype analysis

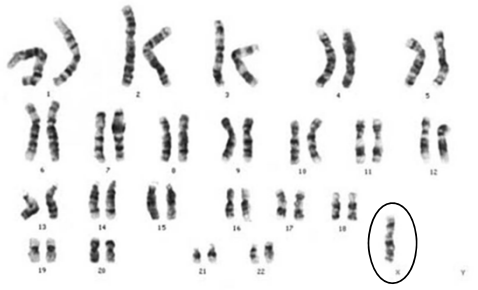


46,XX

Full karyotype analysis

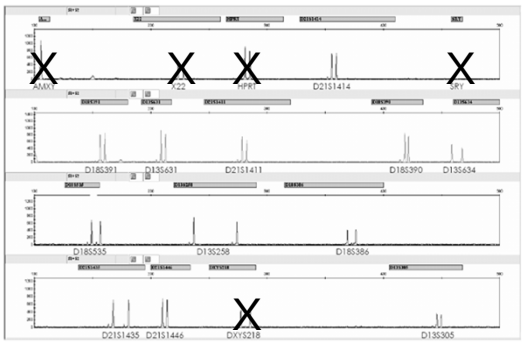
47,XXY

Full karyotype analysis



45,X

QF-PCR



46,X?

Do parents / doctors want to know of these syndromes? & why?

X
Y
?

Routine inclusion in prenatal tests?

Invasive Prenatal Testing for indication "advanced maternal age":

Incidence of Down syndrome increases with maternal age

Incidence of other syndromes are often not related to maternal age

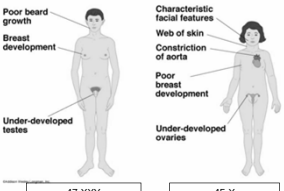
→ ***unexpected finding*** in tests designed to exclude Down syndrome!

Invasive Prenatal Testing for indication "advanced maternal age":

→ Down syndrome?

"unexpected findings"

Sex chromosomal aneuploidies



47,XXY
Klinefelter syndrome

45,X
Turner syndrome

Other X-Y aneuploidies:
eg: 49,XXXXY, etc

Invasive Prenatal Testing

Goal: the exclusion of Down syndrome: 47, XY +21

= a syndrome well known:

1:380 newborns

"**unexpected** findings": aneuploidy of X or Ys:

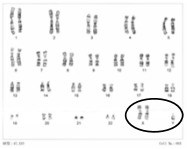
= syndromes unfamiliar to parents!

1:400 newborns!

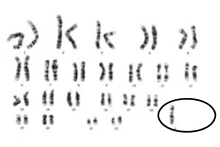
Sex chromosomal aneuploidies:
45, X Turner
47,XXY Klinefelter
47,XXX Triple X
47, XYY 'super male'
48,XXXY
49, XXYY; etc

Most important: uncertain prognosis...!!

Most common sex chromosomal aneuploidies:



47,XXY
Klinefelter syndrome



45,X
Turner syndrome

47,XXX
Triple X syndrome

Table 2: Categorization of disease-specific QOL domains related to SCA

domain I - physical health	growth and bone mineral density
	cardiovascular, metabolic and other disease
	auto-immune disease
	other SCA-associated health problems
	overall disease susceptibility and mortality
domain II - behavior	psychosocial functioning
	quality of life
	sexuality
domain III - reproductive health	puberty
	fertility
	assisted reproduction techniques
	disease

Incidental prenatal diagnosis of sex chromosome aneuploidies: health, behaviour and fertility A systematic descriptive review. ISRN Obstetrics and Gynecology, 2011:807106

47,XXY
Klinefelter syndrome

OR ...

45,X
Turner syndrome

OR ...

47,XXX
Triple X syndrome

??
How affected
will be
the
child's phenotype
??

1. what is the impact of unexpected findings on parents

2. what are their preferences

3. what are the opinions of the treating professionals

"Qualitative research is likely the next step in learning more about the psychosocial, educational, and support needs of these couples."

Christian et al.
PRENATAL DIAGNOSIS 2000

Qualitative research

Essence and Requirements:

- ***systematic and transparent approach***
- ***carefully coding of the data***
- ***discerning and documentation of themes in a consistent and reliable way***
- ***theoretical and practical training***
- ***transcription and analysis supported by software***

Qualitative research

- **Semi-structured** and in-depth interviews
- **Length:** 1.5 - 2 hours
- **How many interviews are enough?**

*•concept of "**saturation**," or the point at which no new information or themes are observed in the data.*

•saturation usually occurs within 6-12 interviews

Guest G, Bunce A, Johnson L. How many interviews are enough? An experiment with data saturation and variability. Field Methods. 2006; 18(1): 59–82.

Retrospective qualitative study

Semi-structured interviews with parents who have been confronted with a sex chromosomal aneuploidy as unexpected finding

parents who continued and those who terminated pregnancy

&

Investigation of professional perspectives

Interviews and questionnaire

Study population

parents that were confronted with an *unexpected finding* in prenatal testing for advanced maternal age:

Not DS but SCA

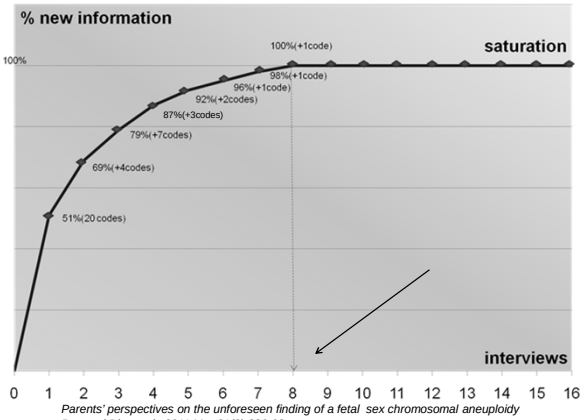
Parents who continued pregnancy	**Parents who chose termination**

Parents that decided continuation of pregnancy

Invited for interview:

Parents who continued pregnancy	**Parents who chose <u>TOP</u>**
n = 17 couples	n = 10 couples
interviewed 8: <u>16 separate interviews</u>	interviewed 5: 10 separate interviews
moved abroad: 2 couples	No reply/ no wish to be interviewed: 5
no wish to participate: 4 couples	
no reply: 3 couples	

Saturation reached after 8 interviews



Parents' perspectives on the unforeseen finding of a fetal sex chromosomal aneuploidy Prenatal Diagnosis 2011 Mar;31(3):286-92

Results of this study

Themes:

I. **Communication of unexpected test result**

II. **Decision-making process**

III. **Child & future**

Theme I: Communication of unexpected findings

Quote:
" The information the doctor gave me on the telephone was very overwhelming and frightening to me. Later I was angry when I understood that it was not at all such a serious handicap".

- **unexpected telephone call, while waiting for reassurance letter**
- **feelings of shock and distress, even anger**
- **no comprehension of information, due to emotions**

Theme II: Decision-making process

Quote:
"It would have been much better if a doctor had been present to explain things and answer our questions while we were searching for information on the Internet; because we found the information rather frightening."

- **unguided search for extra information on the Internet**
- **perceived adequacy of post-test counseling is good**
- **no important role for general practitioner**

Theme III: Child & future

Quote:
"I really don't know if she will be followed or not. I am not sure if this will be organized from the hospital or that we have to make an appointment ourselves. I think I have a letter somewhere, but I don't know where."

- **faith in good quality of life for child**
- **concerned about infertility, stature and health**
- **not much knowledge on psychosocial problems**
- **need for extra support**

Topics for discussion

- **Parents that continued pregnancy after unexpected finding SCA**
- Organisation of pre-test counseling
- Communication of unexpected findings
- The Internet
- Postnatal support programs not evident

Parents that decided Termination Of Pregnancy

Invited for interview:

Parents who continued pregnancy

n = 10 couples

interviewed 5: 10 separate interviews

Saturation reached after 8 interviews!

Parents who chose <u>TOP</u>

n = 10 couples

interviewed 5: 10 separate interviews

No reply/ no wish to be interviewed: 5

Saturation reached after 8 interviews!

<u>Results</u>

Themes:

I. **Perspective parents before the test**

II. **Perspective parents after the unexpected finding**

III. **Reasons for decision to terminate pregnancy**

Theme I: Perspective parents before the test

- **decision before testing to terminate if an abnormality would be found**
- **reason for the test was exclusion of Down syndrome**
- **trusting that the test result would be reassuring**

Theme II: Perspective parents after the unexpected finding

- **unguided Internet searches for extra information**
- **syndrome is unfamiliar but perceived as very burdensome**

Theme III: Reasons for decision to terminate pregnancy

- **no faith in good quality of life for child**
- **much focus on psychosocial problems**
- **would take the same decision if this would happen again**
- **the reason for termination primarily considering the childs' perspective:2/9**
- **the reason for termination primarily considering the parents' own perspective: 7/9**

What is the opinion of professionals?

A: Semi-structured interviews with experts (n=16)

Gynaecologists
Pediatricians-endocrinologists
Psychologists/ psychiatrists
Fertilitysspecialists (gynaecologists en urologists)

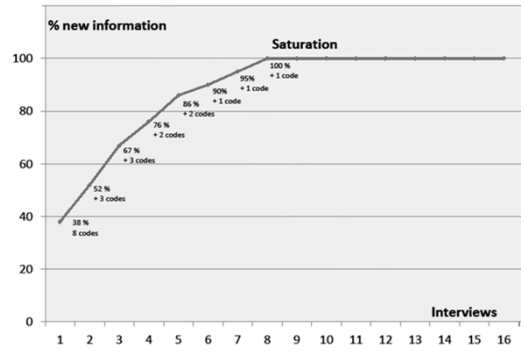
&

B: Questionnaire for clinical geneticists and genetic associates (n=13)

Central question:

Is an incidental prenatal diagnosis of a sex chromosomal aneuploidy a benefit or is it harmful to parents and child?

interviews with professionals



Experts' opinions on the benefit of an incidental prenatal diagnosis of sex chromosomal aneuploidy: a qualitative interview survey. Prenatal Diagnosis 2012 Oct (32):1151-1157

Conclusion interviews with experts and questionnaire

Positive views:

Early psychosocial treatment possibilities

Early medical and preventive treatment possibilities (hormonal substitution or medication)

Better understanding of the child, therefore a better parental/ child relationship and acceptance

Critical views:

Difficult counseling because of large variation in phenotype

Dilemmas for the parents: to continue pregnancy or to terminate

Risk of stigmatision of the child
(experts have an important task in guiding parental attitude towards the child!)

Conclusion interviews with experts and questionnaire

Notwithstanding the complexity of the prenatal counseling and the dilemmas for the parents

→

Prenatale diagnosis of SCA is a benefit for parents and child.

Conclusion

Parents' and professional perspective of unexpected prenatal diagnosis of fetal sex chromosomal aneuploidy

⇩

SCA is unfamiliar and a shock to be unexpectedly confronted with

There is much need for guidance

The benefits greatly outweigh the disadvantages!

Learning objectives

- unexpected findings in prenatal tests: what are the incidences?
- new techniques are able to avoid unexpected findings, is that advisable?
- prenatal finding of a sex chromosomal aneuploidy: what is the prognosis for the child?
- pre- and post-test counseling: what is the role for the professional?
- parental decision-making, what are there emotions, how do they decide?

On seeking and finding the evidence…

- How do patients perceive evidence in prenatal testing?
- What is the role of communication in translating the prenatal diagnosis to parents?
- How do they seek more evidence?
- How do they value professional advice?
- What is important in their decision-making?

COMMUNICATION!!

COMMUNICATION!!

COMMUNICATION!!

COMMUNICATION!!

Summary

- **Unexpected findings in prenatal tests:**
  More common than generally known
  Not unexpected for the professional,
  Thus: should be addressed in pre-test counseling!

- **New techniques are able to avoid unexpected findings**:
  Possibly advisable after counseling of parents

In case of SCA:
parents and professionals thought that the unexpected finding was a benefit

Summary

- **Prenatal finding of a sex chromosomal aneuploidy:**
  Uncertain prognosis for the future child
  Medical, psychological and fertility not certain but preventive measures useful

- **Pre- and post-test counseling**:
  Very important role for the professional

- **Parental decision-making**:
  Personal situation and feelings, combined with professional information

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ESHRE Meeting 2014

The Placebo Effect

Prof. dr. Andrea Evers
Health, Medical, and Neuropsychology

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The Netherlands

ESHRE Meeting 2014

Disclosure

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of Pfizer / Wyeth in the period 2006-2014.
No other pharmaceutical grants.

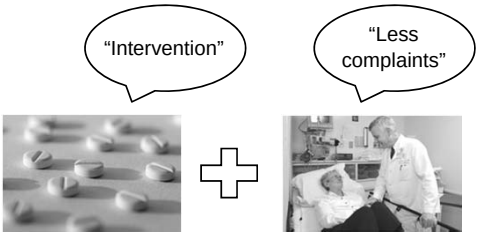
Prof. dr. Andrea Evers
Health, Medical, and Neuropsychology

Universiteit Leiden
The Netherlands

Learning Objectives

1. **To know what placebo and nocebo effects are**
2. **To get insight into the way how expectations mechanisms of placebo and nocebo effects work**
3. **To understand the biopsychosocial factors that influence placebo and nocebo effects**
4. **To recognize the impact of placebo and nocebo effects for clinical practice**

Role of expectations



Leiden University. The university to discover.

Role of expectation mechanisms

Placebo effect

- Favorable treatment effects
  not attributed to treatment mechanism
- Induced by expectations with regard to improvement
  e.g. pain already reduces when seeing the painkiller

Benedetti 2008; Price 2008

Leiden University. The university to discover.

Role of expectation mechanisms

Nocebo effect

- Unfavorable treatment effects
  not attributed to treatment mechanism
- Induced by expectations of worsening
  e.g. I always react sensitive to medicines

Much less attention to nocebo than placebo effects
in spite of high clinical relevance

Benedetti 2008; Price 2008

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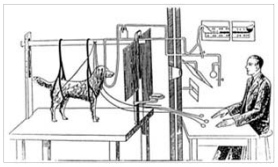
Role of expectation mechanisms

Learning principles

- verbal suggestion
- conditioning



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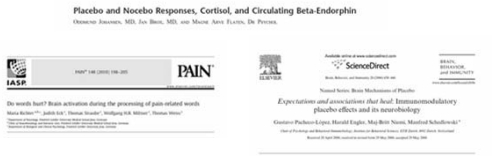
Role of expectation mechanisms in chronic physical symptoms

- Corresponding brain areas activated for pain stimuli induction and only pain expectation
- Expectation effects related to HPA-axis- and immune activity


Placebo and Nocebo Responses, Cortisol, and Circulating Beta-Endorphin

Do words hurt? Brain activation during the processing of pain-related words

Expectations and associations that heal: Immunomodulatory placebo effects and its neurobiology

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Role of expectation mechanisms in chronic physical symptoms

Parkinson patients produce dopamine in dorsale motor striatum after application of placebo-medication

Expectation and Dopamine Release: Mechanism of the Placebo Effect in Parkinson's Disease
Raúl de la Fuente-Fernández, *et al.*
Science **293**, 1164 (2001);
DOI: 10.1126/science.1060937

Research report

Dopamine release in human ventral striatum and expectation of reward

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Role of expectation mechanisms

Table 1 Summary of the mechanisms of placebo and placebo-related effects across diseases/systems and treatments

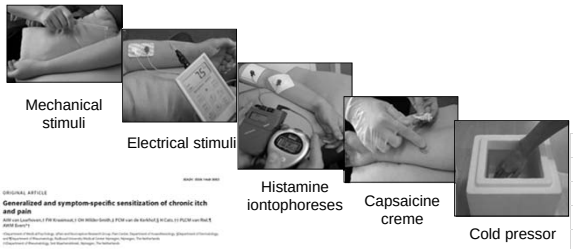
Disease/System	Treatment	Mechanism
Pain	Placebo administration Nocebo administration Verbal suggestions Open versus hidden administration	Expectation-induced activation of endogenous opioids and cholecystokinin as well as of several brain regions
Parkinson's disease	Placebo administration Nocebo administration Verbal suggestions Open versus hidden administration	Expectation-induced release of dopamine in the striatum and changes of firing pattern of subthalamic nucleus neurons
Depression	Placebo administration	Changes of metabolic responses in different brain regions (inhibition of serotonin reuptake?)
Anxiety	Placebo administration Open versus hidden diazepam	Change of activity of some brain regions
Addiction	Expected versus unexpected methylphenidate	Changes of metabolic activity in different brain regions
Autonomic responses to deep brain stimulation	Open versus hidden deep brain stimulation	Change of neuronal excitability in associative/limbic regions
Cardiovascular system	Placebo administration	Reduction of β-adrenergic activity of the heart
Respiratory system	Pharmacological preconditioning with buprenorphine	Conditioning of opioid receptors in the respiratory centers
Immune system	Pharmacological preconditioning with immunosuppressive drugs (e.g., cyclophosphamide and cyclosporin A)	Conditioning of some immune mediators (e.g., IL-2, IFN-γ, lymphocytes)
Endocrine system	Pharmacological preconditioning with 5-HT_{1B-1D} receptor agonists (sumatriptan)	Conditioning of some hormones (e.g., growth hormone, cortisol)

Benedetti, Ann Rev Pharma Tox 2008

Role of expectation mechanisms

Role of expectation mechanisms

Induction of itch and pain in the laboratory:
Quantitative Sensory Testing (QST)



Mechanical stimuli

Electrical stimuli

Histamine iontophoreses

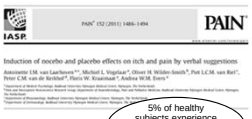
Capsaicine creme

Cold pressor

ORIGINAL ARTICLE

Generalized and symptom-specific sensitization of chronic itch and pain

Role of expectation mechanisms: Verbal suggestions

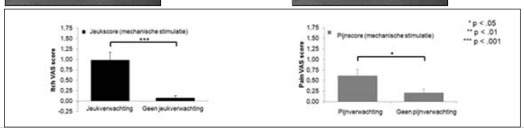


High expectation

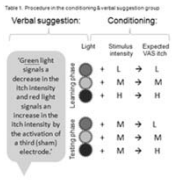
95% of healthy subjects experience itch (pain) by these stimuli

Low expectation

5% of healthy subjects experience itch (pain) by these stimuli



Role of expectation mechanisms: The role of conditioning and verbal suggestions



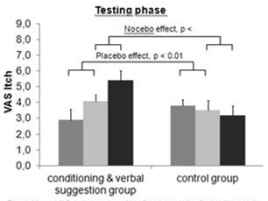
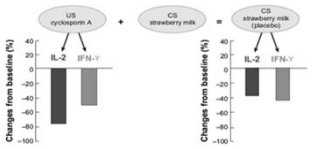


Fig. 1. Mean VAS itch scores of the first green, the first yellow and first red stimulus in the testing phase for both experimental conditions

Bartells et al, 2014, Plos One

Pathways to innovative treatments

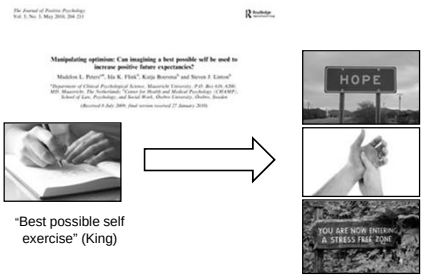
Conditioning of placebo effects
in animal experiments and humans, e.g. immune conditioning



Benedetti, Ann Rev Pharma Tox 2009

Pathways to innovative treatments

Expectancy interventions: Positive imagination



"Best possible self exercise" (King)

Leiden University. The university to discover.

Pathways to innovative treatments

Treatment expectancy interventions

What are the effects of **trainings** for

implicit and explicit **treatment expectancies** for medicines ?

Fear of side effects

Adherence / treatment beliefs

Conditioning of bodily reactions

Leiden University. The university to discover.

Implications for clinical practice

Information about side effects

Doctor-patient communication

Trust in care

Leiden University. The university to discover.

Implications for clinical practice

Physical reactions before starting regular therapy

Nausea before taking medications

Leiden University. The university to discover.

The art of medicine

Prof dr. Jan A.M. Kremer
Nijmegen, The Netherlands

@JKNL, jan.kremer@radboudumc.nl

On seeking and finding the evidence
PCC 6, Munich, 29 June 2014

eshre
Science Moving People Moving Science

Radboudumc

Potential conflicts of interest

- Professor in patient-centred innovation, Radboud University Medical Centre, Nijmegen (NL)
- Consultant Strategy&, Amsterdam (NL)
- Member of the Advisory Committee of the Dutch Quality Institute

Learning objectives

- Medicine is not about 'what doctors do', but about 'what patients need'
- Know some examples of patient paricipation in our field
- Know the recent trends in the art of medicine
- Acknowledge the importance of person based medicine

Gynaecologist Radboud IVF team

Inspired by patients

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Heyendael Castle (2001)

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From paradigm shift to dream

Medicine is not what doctors do, but what patients intend

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Patientcentredness (2001)

Being respectful of and responsive to individual patient preferences, needs and values; and ensuring that patient values guide all clinical decisions. *(Institute of Medicine, 2001)*

One of the dimensions of Quality of Care:

1. *Safety*
2. *Effectiveness*
3. *Efficiency*
4. *Timeliness*
5. *Equity of access*
6. *Patient centeredness*

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Intermezzo (1)

What is according to you the most important dimension of Quality of Care?

1. *Safety*
2. *Effectiveness*
3. *Efficiency*
4. *Timeliness*
5. *Equity of access*
6. *Patient centeredness*

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Dimensions of patientcentredness

1. Access to care
2. Respect for patient's values, preferences, needs
3. Coordination and integration of care
4. Information, communication and education
5. Physical comfort
6. Emotional support and alleviation of fear and anxiety
7. Involvement of family and friends
8. Transition and continuity

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Digital IVF clinic (2003)

General information 1.0
interviews, education leaflets

Personal Health Record
lab results, pictures, letters

Communication
chat and forum (P2D & P2P)

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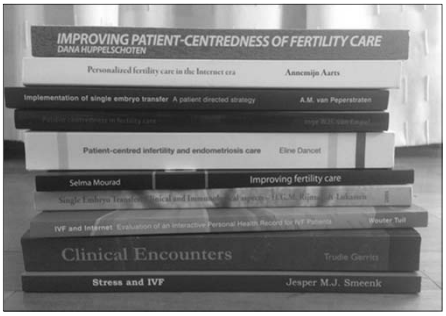
Patient-centred PhD thesis



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Patient-centred PhD thesis

1.	Virtual IVF Clinic	Wouter Tuil
2.	Clinical encounters in fertility care	Trudie Gerrits
3.	Stress and IVF (1)	Chris Verhaak
4.	Stress and IVF (2)	Jesper Smeenk
5.	Shared decision making in SET/DET	Arno van Peperstraten
6.	Guideline implementation by patients	Selma Mourad
7.	Health Communities in fertility care	Annemijn Aarts
8.	Patient-centredness questionnaire NL	Inge van Empel
9.	Patient-centredness questionnaire EU	Eline Dancet
10.	Patient-centredness improvement	Dana Huppelschoten
11.	Patient education via wiki's	Tom van de Belt
12.	Guideline development via wiki's	Elvira den Breejen
13.	Self-management of stress/anxiety	Angelique van Dongen
14.	Personal communities, infertile women	Helga Schouten
15.	Personal communities, pregnant women	Carola Groenen

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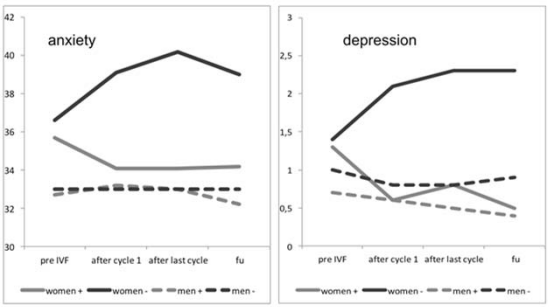
Anxiety and depression after IVF



Verhaak et al HR 2005

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Screen IVF

Hum. Reprod. Advance Access published September 20, 2012
Human Reproduction, Vol.0, No.0 pp. 1–9, 2012
doi:10.1093/humrep/des324

human reproduction ORIGINAL ARTICLE *Psychology and counselling*

Feasibility of screening patients for emotional risk factors before *in vitro* fertilization in daily clinical practice: a process evaluation

A.J.C.M. Van Dongen*, J.A.M. Kremer, N. Van Sluisveld, C.M. Verhaak, and W.L.D.M. Nelen

Department of Obstetrics and Gynecology, Radboud University Nijmegen Medical Centre, PO Box 9101, 6500 HB, Nijmegen, The Netherlands

*Correspondence address. E-mail: a.vandongen@obgyn.umcn.nl

Submitted on January 28, 2012; resubmitted on August 2, 2012; accepted on August 7, 2012

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Digital coach

Self management to reduce stress and anxiety during IVF

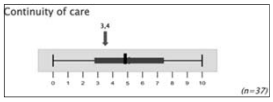
Angelique van Dongen

Radboudumc

Patient Centredness Questionnaire

National tool
- Empel *et al.*, Hum Reprod 2010

International tool
- Dancet *et al*. Hum Reprod 2012



humrep.oxfordjournals.org; www.umcn.nl/pcqinfertility

Doctors underestimate patientcentredness

Discrete Choice Experiment (925 patients and 227 doctors)

Willingness to trade-off pregnancy rate for more patientcentredness

		patients	doctors
Attitude	Friendly and interested	9.8% (9.2; 10.9)	6.3% (4.9; 6.7)
Information	Clear and customized	9.6% (9.0; 10.8)	5.5% (4.1; 5.8)
Continuity	Always seeing own doctor	4.0% (3.5; 4.7)	2.6% (2.0; 3.2)

Inge van Empel, Hum Reprod 2011

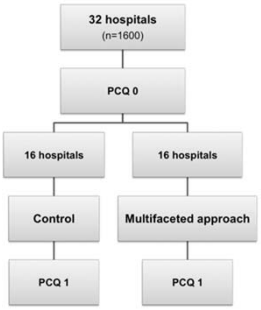
Improving patientcentredness (1)

Cluster randomized trial (n=1620) with a multifaceted approach

- Feedback report
- Educational outreach visits
- Patient-mediated interventions

QUISS
Improving Patient-Centredness

Dana Huppelschoten

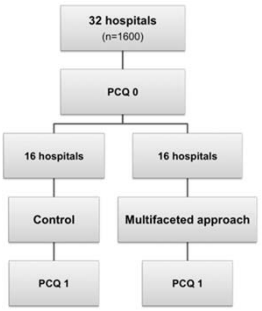


Improving patientcentredness (2)

Cluster randomized trial
- No effect on patientcentredness
- Some effects in sub-dimensions

Process analysis
- Team climate +
- Involvement patients +
- Structured meetings --

Dana Huppelschoten, submitted



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Monetary value of patientcentredness

Discrete Choice Experiment

		1% higher pregnancy rate		more patientcentredness	
	n	Median	(range)	Median	(range)
PATIENTS	*461*	€107	(36-187)	€463	(157-810)
Age					
<36 years	*359*	€80	(36-107)	€346	(157-463)
≥36 years	*102*	€117	(42-187)	€509	(183-810)
Ethnicity					
Dutch	*401*	€107	(49-187)	€463	(214-810)
Non-Dutch	*60*	€49	(36-79)	€212	(157-340)
Income					
Low income	*99*	€59	(36-77)	€254	(157-331)
High income	*362*	€107	(47-187)	€463	(203-810)
Treatment type					
Non-ART	*148*	€80	(36-117)	€346	(157-509)
ART	*313*	€107	(41-187)	€463	(177-810)
HEALTH INSURERS	*45*	€60	(27-150)	€191	(87-477)

Dana Huppelschoten, submitted

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Shared decision making

One or two embryos during IVF?

- RCT with decision aid and choice talk as intervention
- In the intervention-group significantly more decisions for the wise and cost-effective choice of one embryo

Peperstraten: BMJ 2010: 340:c2501

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Wiki's as tools for patients

Patient education leaflets

Tom van de Belt

J Med Internet Res 2013

Guideline development

Elvira den Breejen

J Med Internet Res 2012

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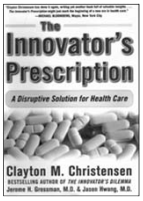
Healthcare crisis

The society wants better care at lower costs

Sustaining innovations
- based on the current paradigm
- make things better and more expensive

Disruptive innovations
- based on a new paradigm
- make things simpler and more affordable



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Person Based Medicine

The patient as a person will be the new paradigm for medicine

1. Call for human touch
2. Call for meaningful work
3. Cost explosion
4. Personalised medicine
5. Internet revolution

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1. Call for human touch

Don Berwick, 2009

2. Call for meaningful work

Annals of Internal Medicine

Established in 1927 by the American College of Physicians

Home | Current Issue | All Issues | Online First | Collections | In the Clinic | Journal Club

6 May 2003, Vol 138, No. 9>

Email | Share | Get Citation

Medical Writings | 6 May 2003

What Do Doctors Find Meaningful about Their Work?

Carol R. Horowitz, MD, MPH; Anthony L. Suchman, MD; William T. Branch Jr., MD; and Richard M. Frankel, PhD

[+] Article and Author Information

Ann Intern Med. 6 May 2003;138(9):772-775 Text Size: A A

Article | References | Comments

Although medical practice has always been difficult and the risk for burnout close at hand, most practitioners have found that the joys and satisfaction of their work have prevailed over the challenges, enabling them to sustain a lifelong commitment to service. Thirteen years ago, we began to conduct workshops to help practitioners reflect on their own experiences in practice and discover and explicitly identify what it is about the practice of medicine that is meaningful to them. We believed that with a rich understanding of what nourished and sustained them, clinicians could attend more consciously and intentionally to enhancing that which was meaningful and attenuating that which was depleting.

COM-Passion For Care

Our work is too much:

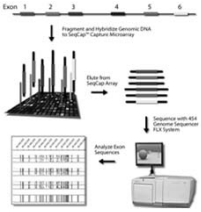
- Standardized
- Fragmented
- Depersonalized

3. Cost and volume explosion

Patients as partners

- self management
- wise decisions
- acceptation at the micro-level
- support at the macro-level

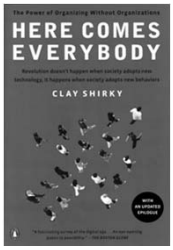
4. Personalized medicine



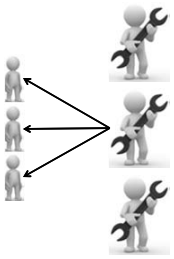
Authority Based Medicine (ABM)
Mechanism Based Medicine (MBM)
Evidence Based Medicine (EBM)
Person Based Medicine (PBM)

5. Internet revolution

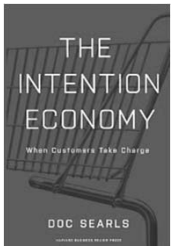
Agile participatory networks
Consumers will be producers



5. Internet revolution

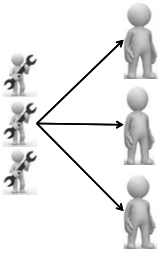


CRM
Customer Relationship Management

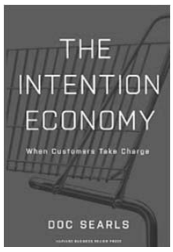


Customers Vendors

5. Internet revolution



VRM
Vendor Relationship Management



Customers Vendors

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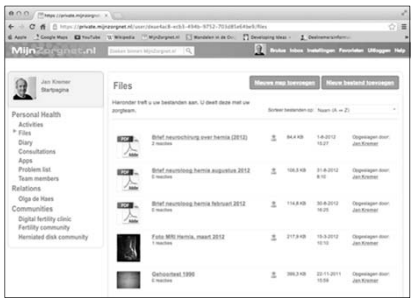
Personal Health Communities



MijnParkinsonZorg

FertiScreen

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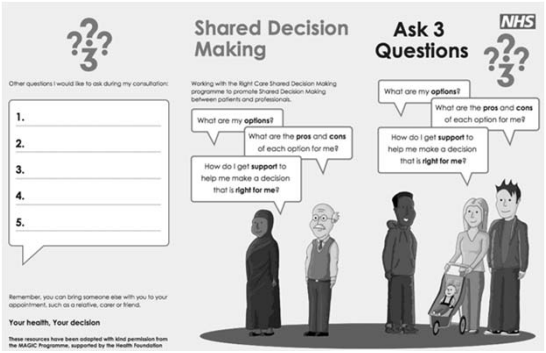

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The world is changing

The new doctor:
- from god to guide
- from host to guest (Don Berwick)

The new patient:
- from passive object to active subject
- from patient to person (TIFKAP)

The new medine:
- from what doctor's do to what patients need
- from

The Individual Formerly Known As Patient

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Next steps in fertility care

Do not overplan
take babysteps

Voyage of discovery
Based on PBM

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The Mindfulness Based Program for Infertility: evidence regarding its efficacy

Ana Galhardo - PhD, Clinical Psychologist

ESHRE Pre-Congress Course

"**On seeking and finding the evidence**"

Munich, 29th June 2014

Disclosure

- I have no conflicts of interest.

Summary

- Brief review of what is known about psychological interventions targeting infertile patients
- Evidence on the efficacy of mindfulness based interventions
- Presentation of the Mindfulness Based Program for Infertility (MBPI)
- Efficacy study of the MBPI

Learning objectives

- Be aware of the importance of psychological intervention in infertility
- Learn about the Mindfulness Based Program for Infertility (MBPI)
- Understand how the development of mindfulness and acceptance skills may be useful for infertile people
- Learn about efficacy results of the MBPI

Psychological consequences

- Infertility has been described as a stressful condition not only from a medical perspective but also in terms of psychological burden, with couples stating that it corresponds to a very demanding life crisis (e.g., Menning, 1980; Burns & Covington, 2006, Wischman et al., 2001)
- Studies addressing the psychological consequences of infertility have been produced mixed results (Chen et al., 2004; Eugster & Vingerhoets, 1999; Greil, 1997; Verhaak et al., 2010; Verhaak & Smeenk, 2007; Volgsten et al., 2008)
- Most couples are able to adjust and cope with infertility but others present problematic emotional responses such as depression and anxiety (Ramazanzadeh et al., 2009)

Psychological interventions
(Burns & Covington, 2006)

- Information Delivery (Daniluk, 1988; Takefman, 1990)
- Emotion and Problem Focused Interventions (McQueeney et al., 1977)
- Support Groups (Ferber, 1995)
- Psychological and Sexual Counseling (Sarrel & DeCherney, 1985)
- Couple Therapy (Diamond et al., 1999; Stammer et al., 2002)
- Cognitive-Behavioral Therapy (Tuschen-Caffier et al., 1999)
- Mind Body Therapy (Domar et al., 1992)

Background

- Boivin (2003):
  - Positive results from psychological interventions can occur in feelings of anxiety, tension and worry, more than in depressive symptoms
  - Interventions which emphasize education and skills training are more effective than the ones addressing emotional expression and support
- deLiz & Strauss (2005):
  - Group interventions and individual/couple psychotherapy tend to decrease anxiety and depression
  - Higher pregnancy rate in women who received psychological intervention prior or during their infertility treatment (45%; 18 studies) when compared to the ones in control groups (14%; 6 studies)

Background

- Hammerli et al., (2009):
  - No significant effects were found regarding mental health (depression, anxiety, interpersonal functioning and infertility related stress)
  - Significant effects were found in pregnancy rates in couples who were not receiving assisted reproductive treatments (ART)
  - Women may benefit more from psychological interventions when compared to their male partners

Background

- Baer (2003):
  - Mindfulness based interventions have been applied and proved effective in numerous health problems such as chronic pain, cancer, anxiety disorders, depression, etc.
  - These interventions are designed to reduce suffering and improve health and well-being, and are broadly applicable to many problems
- Ruiz (2010):
  - A review of outcome studies indicates that ACT shows to be efficacious in a wide range of problems (common patterns of experiential avoidance and cognitive fusion)
  - Effect sizes are large and even better at follow-up

Mindfulness Based Program for Infertility
(Galhardo, Cunha, & Pinto-Gouveia, submitted manuscript)

- Developed based on:
  - Mindfulness Based Programs for stress, chronic pain, anxiety disorders, depression (*e.g.* Kabat-Zinn, 1990; Kabat-Zinn, *et. al*, 1992; Williams et al., 2007)
  - Basic principles of Acceptance and Commitment Therapy (ACT; Hayes et al., 1999)
  - Mind Body Program for Infertility (Domar et al., 1990)
  - Clinical experience on the application of mindfulness and acceptance skills

Mindfulness Based Program for Infertility

- Psychossocial intervention in a group format (15 women)
- 10 weekly sessions 2 hour each (men attend 3 sessions)
- Admission: Semistructured clinical interview and self-report instruments

Mindfulness Based Program for Infertility Skills trained

- Mindfulness

Development of willingness/acceptance through a process of contacting the present moment and be in touch with the unfolding experience in an open and non-judgmental way

Mindfulness practice allows bringing awareness to internal and external experiences as they occur in the moment (Luoma et al., 2007)

Mindfulness Based Program for Infertility Skills trained

- Acceptance/Psychological flexibility

Acceptance, willingness and openness to painful private events (thoughts, feelings, bodily sensations) without trying to suppress, modify or control them

Embracing of a new attitude towards private events, promoting their observation, decentering and non-reacting

Mindfulness Based Program for Infertility Skills trained

- Values clarification
- Interpersonal communication
- Self-compassion and compassion
- Coping strategies

- Psychosocial education on:
  - Lifestyle and fertility (exercise, nutrition, caffeine, alcohol, nicotine and herbal remedies, etc.)
  - Stress, anxiety and depression

Mindfulness Based Program for Infertility

- Materials:
  - Therapist's Manual
  - Participant's Manual
  - CD with mindfulness practice instructions
  - Progress notes
  - Self-report instruments

MBPI- Sessions

- Half-hour of sharing (optional)
- Formal mindfulness practice is held, followed by sharing
- Informal mindfulness practice is also presented
- The “three minutes breathing space” ends each session
- Metaphors and experiential exercises are included in most of the sessions:
  - An experiential exercise of listening to others
  - Introduction of values clarification (valued life directions) through the imagery exercise "10 years of marriage"
  - Integration of a greater number of positive aspects in day-to-day experience

MBPI- Sessions

- Use of metaphors such as "the mind as a radio always on", "the coach and passengers“, “the gardening metaphor”
- Importance of values clarification and committed action (exercise for values identification)
- Exercise “the pain in my head”

MBPI – Sessions 1, 6 and 8

- Session 1 – Participants introduce themselves; program objectives and functioning; buddy assignments; handouts distribution
- Session 6 – *Hatha Yoga*; “The Joy of Stress” video with Loretta LaRoche; “Life map”; Couples’ communication exercise; *Mindfulness* listening to classical music
- Session 8 – Invited couples: a couple who adopted, another one that had gamete donor(s), and a couple who chose to remain childless (or childfree)

Between sessions

- Mindfulness (audio CD) – formal practice
- Mindfulness –informal practice
- Specific exercises related to the topics addressed during the sessions
- Progress notes

Participants

- 55 women in the MBPI group
- 37 women in the control group
- All married or living with a partner
- Primary infertility diagnosis

Instruments

- ***Beck Depression Inventory*** (BDI; Beck et al., 1961; Portuguese version by Vaz-Serra, & Pio-Abreu, 1973a, 1973b)
- ***State Anxiety Inventory form Y*** (STAI-Y1; Spielberg, 1983, Portuguese version by Daniel, 1996)
- ***Others As Shamer*** (OAS; Goss et al., 1994, Portuguese version by Matos, & Pinto-Gouveia, 2010)
- ***Experience of Shame Scale*** (ESS; Andrews et al., 2002 Portuguese version by Matos, & Pinto-Gouveia, 2010)
- ***Entrapment Scale*** (EE; Gilbert, & Allan, 1998; Portuguese version by Carvalho et al., 2011a)
- ***Defeat Scale*** (DS; Gilbert, & Allan, 1998; Portuguese version by Carvalho et al., 2011b)
- ***Acceptance and Action Questionnaire II*** (AAQ II; Bond et al., 2011, Portuguese version by Pinto-Gouveia et al., 2012)
- ***Self-Compassion Scale*** (SCS; Neff, 2003, Portuguese version by Castilho et al., 2011)
- ***Dyadic Adjustment Scale*** (DAS; Spanier, 1976, Portuguese version by Nobre, unpublished manuscript)
- ***Infertility Self-Efficacy Scale*** (ISE; Cousineau et al., 2006, Portuguese version by Galhardo et al., *in press*)
- ***Frieburg Mindfulness Inventory*** (FMI; Walach et al., 2006; Portuguese version by Pinto-Gouveia & Gregório, unpublished manuscript)

Procedure

- Recruitment - announcement posted at the Portuguese Fertility Association (patients association) website
- Aims of the study, inclusion criteria, participants' role, researchers' obligations and procedure to participate were explained
- All subjects gave their written informed consent
- Participants in the MBPI group and control group completed the set of self-report measures at baseline and after the MBPI
- Participants in the MBPI group also attended a structured clinical interview before admission to the program
- The MBPI sessions were held between May 2009 and May 2010 and according to a previously established rule, women in this group did not miss more than two sessions.

Sample characteristics

	MBPI (n = 55)		**Control Group (n = 37)**		***t* (90)**	***p***
	M	**SD**	**M**	**SD**		
Age	34.87	4.20	33.14	3.94	1.20	**.049**
Years of Education	15.82	2.26	14.84	3.48	1.64	.105
Years of Marriage	6.62	3.57	5.70	3.25	1.25	.215
Years of Infertility	3.35	2.53	3.05	2.44	.55	.584

Results (groups comparison at baseline)

	MBPI_T1 (*N* = 55)		**Control Group_T1 (*N* = 37)**		***t* (90)**	***p***
	M	*SD*	*M*	*SD*		
Depression - BDI	11.02	7.05	11.35	9.27	-.20	.845
Anxiety - STAI-Y1	47.82	13.09	47.57	15.22	.08	.933
External Shame - OAS	22.22	12.09	18.35	11.93	1.51	.134
Internal Shame - ESS	55.40	17.84	52.08	16.21	.91	.367
External Entrapment - ES_ext	8.73	8.72	8.24	8.52	.26	.793
Internal Entrapment - ES_int	6.78	6.35	4.73	5.64	1.59	.116
Defeat - DS	19.05	10.67	18.24	13.02	.33	.744
Experiential Avoidance - AAQ-II	23.91	9.10	23.27	8.57	.34	.736
Self-compassion - SCS_comp	39.65	8.82	41.24	9.29	-.83	.409
Self-judgment - SCS_judg	38.49	10.59	38.78	9.01	-.14	.891
Infertility Self-efficacy – ISE	81.87	24.45	86.35	26.98	-.83	.411
Dyadic Adjustment -DAS	114.56	15.08	118.46	11.69	-1.33	.188

Results (repeated measures ANOVAs)

		MBPI Group (*N* = 55)		Control Group (*N* = 37)		Time			Group			TimeXGroup		
MEASURES	Time	*M*	*SD*	*M*	*SD*	*F*	*p*	η^2p	*F*	*p*	η^2p	*F*	*p*	η^2p
Depression (BDI)	T1	11.02	7.05	11.35	9.27	20.99	.000	.19	2.45	121	.03	8.06	**.006**	.08
	T2	6.18	4.05	10.22	8.79									
Anxiety (STAI-Y1)	T1	47.82	13.09	47.57	15.22	2.22	.140	.02	.99	.323	.01	2.22	.140	.02
	T2	43.02	8.70	47.57	14.22									
External Shame (OAS)	T1	22.22	12.09	18.35	11.93	6.66	.011	.06	.35	.556	.00	5.99	**.016**	.06
	T2	17.09	10.75	18.22	13.26									
Internal Shame (ESS)	T1	55.40	17.84	52.08	16.21	11.41	.001	.11	.02	.877	.00	4.94	**.029**	.05
	T2	48.33	14.91	50.62	17.61									
External Entrapment (ES_ext)	T1	8.73	8.72	8.24	8.52	7.08	.009	.07	.27	.603	.00	5.44	**.022**	.06
	T2	5.85	6.60	8.05	9.18									
Internal Entrapment (ES_int)	T1	6.78	6.35	4.73	5.63	5.55	.021	.06	.38	.540	.00	6.53	**.012**	.07
	T2	4.12	4.86	4.84	5.98									

Results (repeated measures ANOVAs)

		MBPI Group (*N* = 55)		Control Group (*N* = 37)		Time			Group			TimeXGroup		
MEASURES	Time	*M*	*SD*	*M*	*SD*	*F*	*p*	η^2p	*F*	*p*	η^2p	*F*	*p*	η^2p
Defeat (DS)	T1	19.05	10.67	18.24	13.02	7.57	.007	.08	.27	.606	.00	4.27	**.042**	.05
	T2	14.49	8.24	17.59	14.10									
Experiential Avoidance (AAQ-II)	T1	23.91	9.10	23.27	8.57	13.27	.000	.13	.15	.704	.00	2.38	.126	.03
	T2	19.64	7.50	21.54	9.93									
Self-Compassion (SCS_comp)	T1	39.70	8.90	41.24	8.65	1.23	.271	.01	.12	.728	.00	1.77	.187	.02
	T2	41.50	8.72	41.08	9.46									
Self- Judgment (SCS_judg)	T1	38.49	10.59	38.78	9.01	26.34	.000	.23	.21	.641	.00	.93	.338	.01
	T2	34.38	8.70	35.97	11.68									
Infertility Self-Efficacy (ISE)	T1	81.87	24.45	86.35	26.98	18.72	.000	.17	.52	.472	.01	13.88	**.000**	.13
	T2	98.87	19.58	87.62	26.88									
Dyadic Adjust (DAS)	T1	114.56	15.08	118.46	11.69	.69	.408	.01	1.17	.281	.01	.78	.379	.01
	T2	116.38	14.18	118.41	13.03									

Results

- Significant timeXgroup effects were found regarding:
  - Depression
  - External and internal shame
  - External and internal entrapment
  - Defeat
  - Self-efficacy to deal with infertility

  Medium effect sizes

Results MBPI Group (paired samples *t* tests)

	MBPI_T1 (*N* = 55)		MBPI_T2 (*N* = 55)		*t* (54)	*p*	η^2
	M	*SD*	*M*	*SD*			
Depression - BDI	11.02	7.05	6.18	4.05	5.46	**<.001**	.36
Anxiety - STAI-Y1	47.82	13.09	43.02	8.70	2.73	**.009**	.10
External Shame - OAS	22.22	12.09	17.09	10.75	3.44	**.001**	.18
Internal Shame - ESS	55.40	17.84	48.33	14.91	3.95	**<.001**	.21
External Entrapment - ES_ext	8.73	8.72	5.85	6.60	3.62	**.001**	.20
Internal Entrapment - ES_int	6.78	6.35	4.13	4.86	3.20	**.002**	.16
Defeat - DS	19.05	10.67	14.49	8.24	3.37	**.001**	.17
Experiential Avoidance - AAQ-II	23.91	9.10	19.64	7.50	3.56	**.001**	.19
Self-compassion - SCS_comp	39.65	8.82	41.44	8.65	-1.77	**.083**	.05
Self-judgment - SCS_judg	38.49	10.59	34.38	8.70	4.54	**<.001**	.28
Infertility Self-efficacy – ISE	81.87	24.45	98.87	19.58	-6.00	**<.001**	.40
Dyadic Adjustment - DAS	114.56	15.08	116.38	14.18	-1.25	.216	.03
Mindfulness Skills - FMI	34.00	5.05	38.40	5.57	-4.24	**<.001**	.38

Results Control Group (paired samples *t* tests)

	Control Group_T1 (*N* = 37)		Control Group_T2 (*N* = 37)		*t* (36)	*p*	η^2
	M	*SD*	*M*	*SD*			
Depression - BDI	11.35	9.27	10.22	8.79	1.28	.209	.04
Anxiety - STAI-Y1	47.57	15.22	47.57	14.22	.00	1.00	.00
External Shame - OAS	18.35	11.93	18.22	13.26	.12	.904	.00
Internal Shame - ESS	52.08	16.21	50.62	17.61	.94	.351	.02
External Entrapment - ES_ext	4.73	5.64	4.84	5.98	-.24	.804	.00
Internal Entrapment - ES_int	8.24	8.52	8.05	9.18	.25	.813	.00
Defeat - DS	18.50	12.15	15.83	10.10	1.02	.323	.03
Experiential Avoidance - AAQ-II	23.27	8.57	21.54	9.93	1.89	.067	.09
Self-compassion - SCS_comp	41.24	9.29	41.08	9.46	.17	.867	.00
Self-judgment - SCS_judg	38.78	9.01	35.97	11.68	2.98	**.005**	.19
Infertility Self-efficacy – ISE	86.35	26.98	87.62	26.88	-.43	.670	.00
Dyadic Adjustment -DAS	118.46	11.69	118.41	13.03	.04	.970	.00

Results

- Women in the MBPI group significantly:
  - Decreased:
    - **Depressive symptoms**
    - Anxiety symptoms
    - **External and internal shame**
    - **External and internal entrapment**
    - **Defeat**
    - Experiential avoidance
    - Self-judgment
  - Increased:
    - **Self-efficacy to deal with infertility**
    - Mindfulness skills

Results

- Women in the control group significantly:
  - Decreased:
    - Self-judgment

No significant differences were found in any other variables

Discussion

- Participants on the MBPI revealed a significant decrease in terms of depressive symptoms, external shame, internal shame, entrapment and defeat:
  - Depressive symptoms are related to distorted thoughts about one's self and themes of worthlessness and self-blame are rather frequent
  - Defusing from thoughts is one of the skills trained during the MBPI and this may be an important factor for the depressive symptoms reduction (Williams et al., 2007)
  - Depression is also related to entrapment and defeat and our results also show a decrease in these variables

Discussion

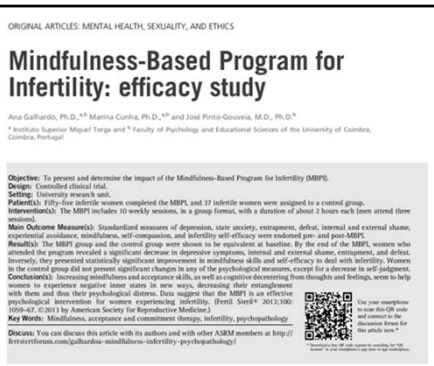
- With the practice of mindfulness skills, participants became more conscious of their internal and external experience in the present moment with an attitude of openness and curiosity. Thus, painful thoughts and feelings related to the past or to the future are recognized without trying to suppress or modify them and this may lead to a decrease of the impact that they might have on depressive symptoms
- As for internal and external shame, MBPI participants seem to perceive themselves less negatively, less inadequate, different, unlovable, or unworthy. They also seem to see themselves as existing in the mind of the others as someone with less negative characteristics, (unattractive, worthless, defective, or inferior), (Gilbert & Allan, 1998; Gilbert, 2002)

Discussion

- They have also developed acceptance skills, and their sense of self-efficacy to deal with infertility:
  - They seem to be more capable of accepting their adverse inner states (*e.g.* feelings, thoughts, bodily sensations) and have more psychological flexibility (Bond et al., 2011; Hayes, 2005), which makes them more capable of conscious and deliberate actions, guided by their values, in a flexible and adaptable way to their circumstances (Harris, 2009)
- Women in the control group did not present significant changes in any of the psychological measures, except for a decrease in self-criticism:
  - This variable corresponds to a sum of isolation, overidentification and self-criticism, we hypothesize that their participation in the study may have provided a sense of not being alone and of doing something positive for others, which may in turn contribute to a less self-critical attitude. Moreover, half of the participants in this group started treatment during the period of the MBPI application, which may have helped them to feel more supported, less isolated and less identified with the problem, since they were doing something to try to solve it

In summary

- MBPI showed to be an effective psychological intervention for women experiencing infertility
- Effects were found on several measures, not only regarding psychopathology, but also in terms of emotion regulation processes, mindfulness skills, and how participants perceive their ability to cope with the demands of infertility and medical treatment
- MBPI is the first program that focuses specifically on mindfulness and acceptance skills designed for people with infertility
- The MBPI can contribute to minimize suffering and negative consequences that infertility and its treatment trigger in these patients, help them to live a more vital, flexible and values-based life and being less focused on infertility



ORIGINAL ARTICLES: MENTAL HEALTH, SEXUALITY, AND ETHICS

Mindfulness-Based Program for Infertility: efficacy study

Ana Galhardo, Ph.D.,[a,b] Marina Cunha, Ph.D.,[a,b] and José Pinto-Gouveia, M.D., Ph.D.[b]

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Objective: To present and determine the impact of the Mindfulness-Based Program for Infertility (MBPI).
Design: Controlled clinical trial.
Setting: University research unit.
Patient(s): Fifty-five infertile women completed the MBPI, and 37 infertile women were assigned to a control group.
Intervention(s): The MBPI includes 10 weekly sessions, in a group format, with a duration of about 2 hours each (men attend three sessions).
Main Outcome Measure(s): Standardized measures of depression, state anxiety, entrapment, defeat, internal and external shame, experiential avoidance, mindfulness, self-compassion, and infertility self-efficacy were endorsed pre- and post-MBPI.
Result(s): The MBPI group and the control group were shown to be equivalent at baseline. By the end of the MBPI, women who attended the program revealed a significant decrease in depressive symptoms, internal and external shame, entrapment, and defeat. Inversely, they presented statistically significant improvement in mindfulness skills and self-efficacy to deal with infertility. Women in the control group did not present significant changes in any of the psychological measures, except for a decrease in self-judgment.
Conclusion(s): Increasing mindfulness and acceptance skills, as well as cognitive decentering from thoughts and feelings, seem to help women to experience negative inner states in new ways, decreasing their entanglement with them and thus their psychological distress. Data suggest that the MBPI is an effective psychological intervention for women experiencing infertility. (Fertil Steril® 2013;100: 1059–67. ©2013 by American Society for Reproductive Medicine.)
Key Words: Mindfulness, acceptance and commitment therapy, infertility, psychopathology

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/galhardoa-mindfulness-infertility-psychopathology/

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Galhardo, A., Cunha, M., & Pinto-Gouveia, J. (2013). Mindfulness Based Program for Infertility: Efficacy study. *Fertility and Sterility*, 100, 4, 1059-1067.

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Thank you for your attention!

Any questions?

Additional information

Please email Ana Galhardo

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Yoga: Its potential role in infertility management

Rajvi H Mehta PhD
Chief Scientist, Light on Yoga Research Trust
Director, Trivector Embryology Support Academy
Mumbai, India

Declaration

- I am a student and teacher of yoga at the Light on Yoga Research Trust for the past 30 years.
- This presentation is based on my experiences and knowledge of the subject of yoga.
- I am not involved in any activity which has any conflict of interest.

Learning objectives:

- An introduction to the ancient Indian science of yoga.
- How yoga connects the body-mind-breath-emotions.
- Summary of research on the efficacy of yoga.
- The psychological impact of infertility and on infertility.
- Role of yoga in infertility management - the methodology.

What is yoga?

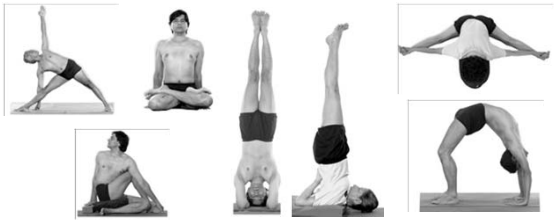
- It is an ancient Indian science and philosophy, which dates back over 2500 years.
- Its practice is said to lead to physical well being, emotional equanimity, mental sharpness and intellectual clarity.
- It is a science which deals with the coordination, communication and communion of the various parts of the body with the mind and the breath.

The eight aspects of yoga

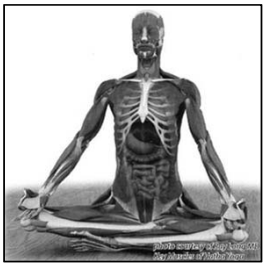
Yama	Social discipline		*Pratyahara*	Involution of senses
Niyama	Moral discipline		*Dharana*	Concentration
Asana	Postures		*Dhyana*	Meditation
Pranayama	Regulation of breath		*Samadhi*	Ultimate bliss

The yoga postures

The human body is moulded into various postures: standing, sitting, inverted, forward & backward extension, supine and twisting.



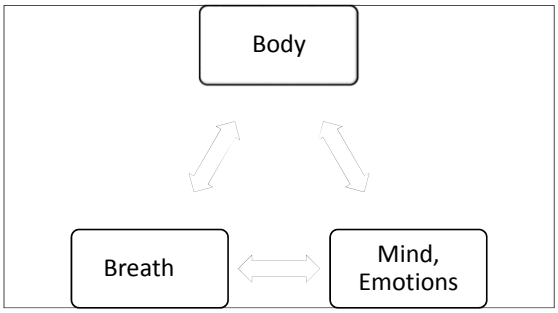
Influence of the asana on the mind



Asanas are examples of bio-engineering where the various parts of the body are placed in unique positions to bring about positive effects through the body on the mind.

Photo courtesy: Dr. Ray Long

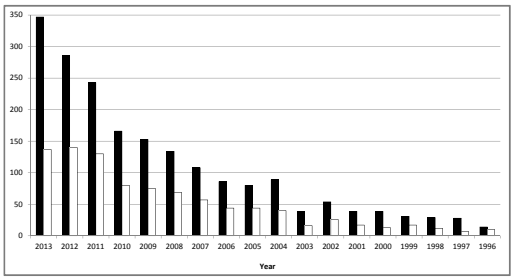
The body - breath - mind - emotion connection while practicing yoga



Yoga in the world today . . .

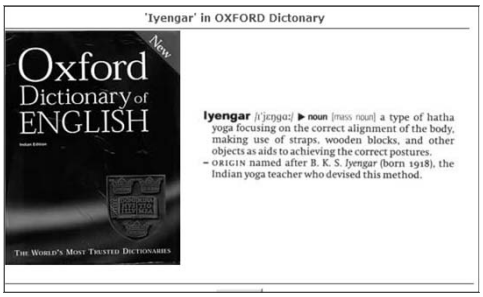
- Re-emergence of interest in yoga in India & the world in the late 20th century.
- Practice has spread from India all over the world.
- Yoga is the 6th most commonly used complementary practice and 6 % of adults use yoga for health reasons. [NHIS 2007]
- The estimated number of yoga practitioners
  - 16.5 million people in US [2005]
  - 2.5 million in Britain [2008]
  - 4 million in Germany [2002]

Research papers on yoga [blue] & yoga therapy [red] per year



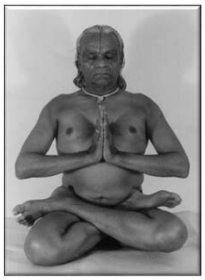
Source: Pubmed

'Iyengar' Yoga



BKS Iyengar – living legend

- 80 years of personal experience.
- Innovative use of props making it possible for all to do the asanas (postures).
- Teachers trained for 5 years.
- Specific sequences designed for different health conditions.
- Reproducible across countries.



Research studies on the efficacy of Iyengar Yoga as 'therapy'

Skeleto- muscular disorders		
Chronic (11 yrs) low back pain	64% reduction in pain 77% reduction in functional disability 88% reduction in pain medication	*Williams et al (2005) Pain 115: 107-117*
Gait disorder in elderly	> 1 cm increase in height Increase in stride length Increase in speed	*DiBenedetto et al (2005) Arch Physical Med Rehabil 86: 1830-1837*
Osteo-arthritis of knee	46% reduction in pain 39% improvement in physical function	*Kolasinski et al. (2005)J Altern Complement Med 11: 689-693*
Rheumatoid arthritis	improvements in pain, pain disability, depression, mental health	Evans et al (2010) J Pain Symptom Manag.39: 904-13.

Research studies on the efficacy of Iyengar Yoga as 'therapy' - II

Physiological functions		
Cardiovascular Risk	Improves BP, heart rate, respiratory rate, decreases HDL levels	Cramer et al (2014) Int. J Cardiol. PMID: 24636547
Hypertension	5 to 8 unit reduction on SBP & DBP as compared to an increase in 'controls'	Cohen et al (2011) Evid Based Complement Alternat Med. PMC 3145370
Arrhythmia	50% reduction in atrial fibrillation episodes	Lakkireddy et al (2013) J. Am Coll. Cardiol. 61:1177
Menopausal Symptoms	30.8% reduction in number of hot flushes	Cohen et al. (2007) Mauritas 56:198.

Research studies on the efficacy of Iyengar Yoga as 'therapy' - III

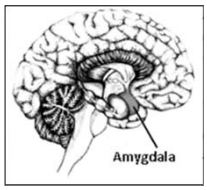
Psychological effects		
Stress Reduction	Improvements in perceived stress, State and Trait Anxiety, well-being, vigor, fatigue and depression	Michalsen et al (2012) Evid Based Complement Alternat Med PMC3463199
Depression	Decreased in self reported symptoms of depression and mood'	Woolery et al (2004) Alt Therap Health Med 10:60-63.
Depression	Decrease in depression symptoms over time [24.9 to 5.67]; decrease in anxiety [12 to 7.33]	Harner et al (2010) Nurs Res. 59:389-99.

Potential mechanism of an emotional effect of yoga postures

- γ Amino butyric Acid (GABA) levels reduced in mood and anxiety disorders.
- 27% increase in brain GABA levels after 60 min yoga.
  - [Streeter et al. (2007) J Altern Complement Med 13:419-26]
- Yoga subjects reported greater improvement in mood and greater decreases in anxiety than a matched walking group.
  - [Streeter et al (2010) J Altern Complement Med 16:1145-1152]

Altered cerebral blood flow

- Anxiety, post traumatic stress disorder and fear increases blood flow to the amygdalal region.
- Practice of yoga decreases blood flow to the amygdalal region.
  - Cohen et al (2009) J Altern Complement Med. 15: 9–14.



Infertility - emotional disorder?

- Frustration
- Inadequacy
- Fear
- Anxiety
- Shame
- Guilt
- Anger
- Depression
- Hope
- Despair

Most couples may express only 'emotional symptoms".

'Symptomatic relief' needs to be provided while the root cause of infertility is being addressed.

Psychological impact OF Infertility

- Mental pressure experienced by infertile women.
- Severe mental stress by 52% of the infertile women
- Psychiatric symptoms (severe depression and anxiety) significantly higher in infertile women as compared with controls.

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Psychological impact ON fertility

- Baseline stress affects the number of oocytes retrieved and fertilized, pregnancy, live birth delivery, birth weight, and multiple gestations.
  - *Klonoff-Cohen et al (2001). Fertil Steril 76: 675-687*
- Men experiencing 2+ stressful life events had lower sperm concentration & lower percent motile sperm
  - *Gollenberg et al (2010) Fertil Steril 93: 1104-1111.*
- Infertility-specific stress (OR = 0.964, p = .011) and nonspecific anxiety (OR = 0.889, p = .006) were negatively associated with pregnancy.
  - Gouranti et al (2011) Women health 51:321-339

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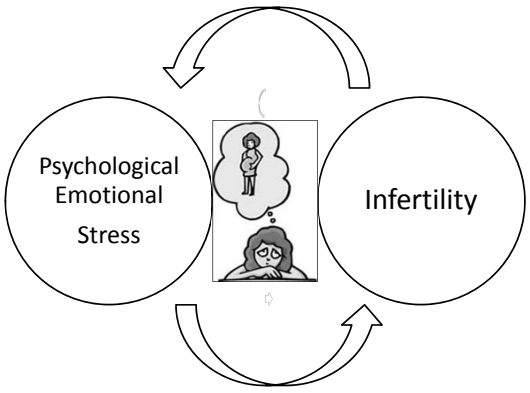
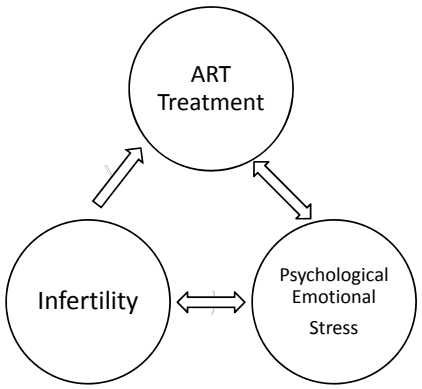




Role of yoga in infertility management

- Decrease stress
- Decrease anxiety
- Prevent depression

- Give emotional strength
  - To accept infertility
  - To 'withstand' infertility treatment.

Aim of yoga during infertility management

The aim of yoga is
to provide freedom from pain
and
bring ease to the state of **dis-ease**!

Approach of yoga

Specific postures performed in specific sequence & retained for specific periods of time aid in alleviating symptoms of dis-ease / disease itself.

Significance of 'right' posture

Researchers /yoga specialists determine

- The asanas to be performed
- The sequence in which to do them
- The duration for which to maintain them

BUT

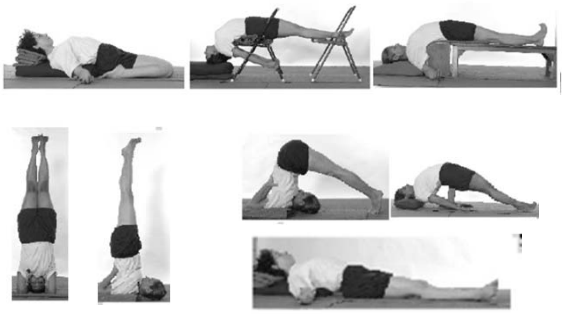
The efficacy of yoga would be determined by the quality of the posture (asana).

Use of props to do the 'right' postures






Yogasanas (postures) for emotional strength

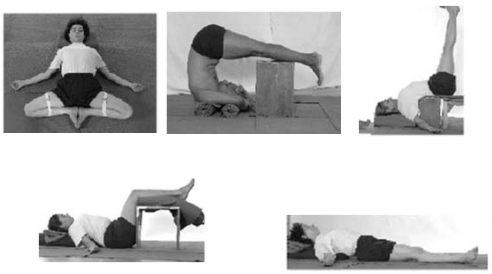


Potential physiological effect of yogasanas in infertile women

? Improve endocrine function
? Stimulate ovaries
? Improve blood flow to the pelvic region

Further studies need to be carried out to determine its efficacy.

Recommended yoga routine during ART Treatment – during stimulation



Recommended yoga routine during ART Treatment – post embryo transfer





- Yoga can be a 'supportive' therapy in infertility management.
- Certified yoga teachers should be involved in guiding the patients with the yoga practice.

UPCOMING ESHRE EVENTS

// ESHRE CAMPUS EVENTS

ESHRE's 30th Annual Meeting

www.eshre2014.eu

Munich, Germany
29 June - 2 July 2014

Epigenetics in reproduction

www.eshre.eu/lisbon

Lisbon, Portugal
26-27 September 2014

Endoscopy in reproductive medicine

www.eshre.eu/endoscopyoct

Leuven, Belgium
15-17 October 2014

Making OHSS a complication of the past: State-of-the-art use of GnRH agonist triggering

www.eshre.eu/thessaloniki

Thessaloniki, Greece
31 October-1 November 2014

From gametes to blastocysts – a continuous dialogue

www.eshre.eu/dundee

Dundee, United Kingdom
7-8 November 2014

Controversies in endometriosis and adenomyosis

www.eshre.eu/liege

Liège, Belgium
4-6 December 2014

Bringing evidence based early pregnancy care to your clinic

www.eshre.eu/copenhagen

Copenhagen, Denmark
11-12 December 2014

An update on preimplantation genetic screening (PGS)

www.eshre.eu/rome

Rome, Italy
12-13 March 2014

For information and registration: www.eshre.eu/calendar
or contact us at info@eshre.eu

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